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Section of Dermatology

President—H. HALDIN-DAVIS, F.R.C.S.

[*November* 17, 1938]

Sjögren's Syndrome associated with Pigmentation and Sclerodermia of the Legs.—J. H. SHELDON, M.D. (Wolverhampton) (introduced by Dr. A. WHITFIELD).

Patient, female, aged 43. Four children, the youngest of whom is now 8 years old. Patient's illness dates from the birth of this child, and the symptoms, which have been slowly progressive, are as follows :—

(1) A completely dry mouth, the tongue and mouth cavity being without any secretion. No saliva is secreted when she is eating, and it is necessary to accompany each mouthful with a sip of water. Injection of 1 c.c. prostigmin produced no saliva, and $\frac{1}{10}$ gr. pilocarpine induced a very slight and transient moisture in the mouth. The submaxillary and parotid glands are palpable as hard swellings about the size of an almond nut.

(2) A similar dryness of the pharynx.

(3) Voice is husky and at times she can only talk in a whisper, on account of dryness of the larynx. Examination by Mr. W. W. Hallchurch (Royal Hospital, Wolverhampton), showed that the vocal cords moved normally, but the mucous membrane of the larynx and surrounding structures was dry and atrophic, and covered with a sticky mucopurulent secretion.

(4) The nose is similarly affected, examination showing a dry atrophic rhinitis with much crusting, and the patient is troubled by ozæna.

(5) The conjunctivæ are also dry, though the severity of this varies from time to time. When it is worse there is much redness of the conjunctivæ, photophobia, and blepharospasm. Vision normal. Fundi normal. Lacrimal glands cannot be palpated.

In addition to these features, which form the characteristic Sjögren's syndrome, there have developed during the same period :—

(1) Mental changes, for which she has been a voluntary inmate in the Staffordshire County Asylum. The symptoms are mostly of a delusional type and are cheerful in character.

(2) Epileptic fits.

(3) An affection of the skin : (*a*) There are a number of small telangiectases on the face. (*b*) Over the thighs small reddish raised spots frequently develop which disappear in a few days' time. (*c*) Both legs show a dark pigmentation which is almost symmetrical, but is rather more marked on the right than the left. It reaches from just below the knees and extends to the dorsum of the feet. The colour has varied somewhat in intensity, but is usually a very dark brown, and at times and in places almost black. It consists of darker points on a less dark background, and is associated with numerous small telangiectases. These appear from time to time, and tend to become covered with thick black crusts. Both soles show hyperkeratosis but are not pigmented. The skin tends to be adherent to the deeper tissues, especially in the lower third of the leg and the dorsum of the feet.

Microscopic examination of the submaxillary gland shows intense fibrosis with almost complete destruction of the gland tissue, and infiltration by round cells.

Histological report on skin from leg (Dr. W. Freudenthal): Epidermis thinned. Sclerodermatous changes in the cutis and especially in subcutaneous trabeculæ. Destruction of elastic fibres in a sharply defined band occupying the upper third of the cutis. Great amount of iron pigment in middle and deeper cutis. Some lymphocytes and plasma cells mainly in the subcutis.

Dr. F. PARKES WEBER said he thought that the condition of the patient's legs was not what was ordinarily called sclerodermia, but resembled what happened in some chronic purpuric conditions (for instance, in the legs of some cases of Cushing's disease and in "orthostatic" pigmentary states of the legs).

In his paper with Dr. A. Schlüter (*Deut. Arch. f. klin. Med.*, 1937, **180**, 333) Dr. Weber, under the heading "Sjögren's syndrome", had tried to separate a process of chronic (mostly non-suppurative) inflammatory fibrosis of the salivary and lacrimal glands from Mikulicz's disease, Heerfordt's syndrome and sarcoid, and true tuberculous affections.

[POSTSCRIPT, 6.1.39.—It is of extraordinary interest that Dr. W. Stahel (*Klin. Wochenschr.*, 1938, **17**, 1692) has succeeded in obtaining an excellent result in a woman, aged 64, with very severe Sjögren's syndrome, by three months' treatment with vitamin A ("Vogan"), 16,000 biological units daily.—F. P. W.]

Two Cases of Diffuse Sclerodermia, Sclerodactylia and Myositis.—G. B. DOWLING, M.D.

I.—Man, aged 40, with severe muscular weakness.

Pathological report (Dr. W. Freudenthal): Right triceps muscle: By lower power several patches are seen in which the muscle-bundles are very faintly stained—with van Gieson—in a pale grey-yellow. By higher power degenerative changes throughout the section are seen. Cross-striation is entirely absent. Many bundles are hyalinized, some show fine vacuoles, others are split longitudinally. In some places the bundles are caked together, in others they show a scalloped border; sometimes the bundles seem to have spread with loss of a definite outline; in some places in the faintly stained patches the bundles have disappeared leaving an empty sarcolemma. The perimysium is slightly increased and is the site of a dense focal lymphocytic infiltration (figs. 1 and 2).

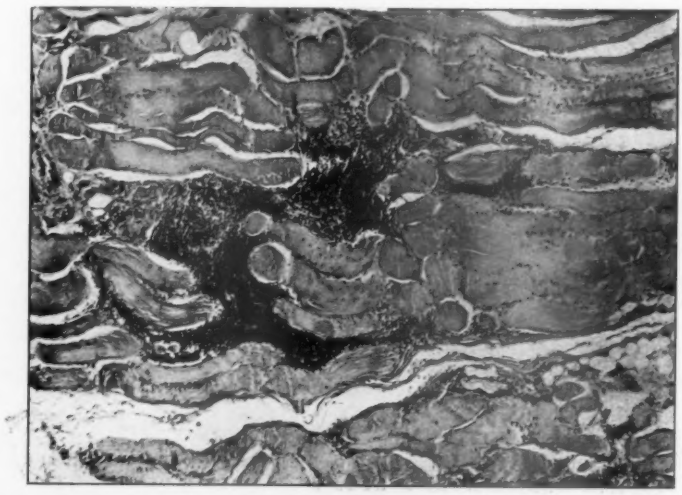


FIG. 1.—Case I. Muscle bundles hyalinized, caked together in places, areas staining faintly. Dense focal lymphocytic infiltration.

FIG. 2.—Case I. Gross disintegration of muscle. Bundles hyalinized, in parts broken to pieces. The bundles are faintly stained in some places; in others (right margin) they have almost disappeared. Cross striation entirely absent.

II.—Woman, aged 55.

Pathological report (Dr. W. Freudenthal): Right thigh muscle: The muscle-bundles have lost their cross-striation in most places. Many bundles are hyalinized, some show a longitudinal splitting, and a few are broken into fragments. Frequently the nuclei are arranged in rows along the sarcolemma. Inflammatory changes are hardly noticeable (fig. 3).

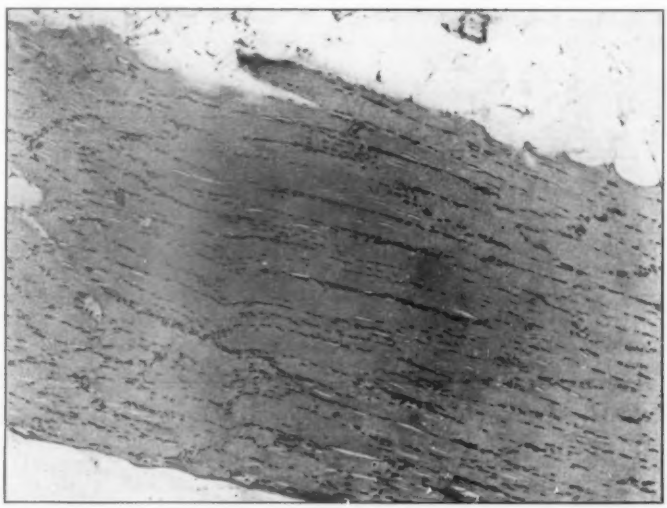


FIG. 3.—Case II. Bundles hyalinized, cross striation absent, nuclei increased and arranged in rows along the sarcolemma.

Comment.—The biopsies came from two patients shown at the June meeting[1] of this year as cases of dermatomyositis. The general opinion then appeared to be that symmetrical sclerodermia with sclerodactylia would be the more appropriate term, and I think that was the right view.

In his description of " diffuse sclerodermia with sclerodactylia " Radcliffe Crocker, under complications, wrote : " Myositis with pain and contractures of the limbs have been repeatedly observed." Under symptoms he says, " the mucous membranes of one or other of the cavities is affected in some instances, including that of the mouth, tongue, palate, pharynx, and œsophagus—to judge from occasional dysphagia ". A few weeks ago Dr. J. A. Nixon sent me reprints of two articles published by him in 1903 and 1907. The first, entitled " Muscular Atrophy and Sclerodermia ", was the report of a case similar to the more severe of my two (the male). In the second, entitled " Sclerodermia and Myositis ", he described three further cases and quoted 15 already reported, including the original one of Petges and Cléjat. He remarked that while muscular atrophy was recognized as common in sclerodermia, he had been under the impression that it was generally thought to be due to invasion of the muscle by contiguous sclerodermia, causing atrophy by compression or strangulation. However, the affected muscles were, for the most part, not overlain by sclerodermatous skin. Dr. Bamber, in a case which he presented here in 1936 (*Proceedings*, **29**, 1635, Sect. Derm., 103), said that he had difficulty in deciding whether it was one of acrosclerosis (Sellei) or dermatomyositis. He decided in favour of the latter because severe muscular atrophy was present in muscle not covered by sclerodermatous skin.

I saw a patient in consultation with Dr. C. P. Symonds over three years ago upon whom the diagnosis of sclerodermia had been made by Dr. MacCormac before any muscular weakness had become evident, but who eventually became bedridden for months owing to weakness involving the greater part of the skeletal muscles as well as those of the palate, pharynx, and larynx ; she also developed marked Raynaud's symptoms. The sclerodermia in this case was relatively superficial. In addition to the two cases from whom the sections shown to-day have been made, I have recently seen a third case of symmetrical sclerodermia with sclerodactylia and Raynaud's symptoms, who was first diagnosed as an obscure œdema. She had slight but definite nasal speech, a voice which had become feebler by degrees, and gross muscular weakness. A fourth, whom I saw in consultation with Dr. Gardiner-Hill, had been diagnosed as sclerodermia in South America. She had the sclerodermic facies, and just detectable sclerodermia of the hands and forearms ; but what worried her most was muscular weakness and abdominal swelling due to œdema without ascites. I saw her eight months ago. She has since improved considerably.

I have quoted all these cases because they appear to me to lend support to the view that I expressed at the June meeting, namely that dermatomyositis and symmetrical sclerodermia with sclerodactylia were related diseases. I believe that what we are in the habit of calling dermatomyositis is really symmetrical sclerodermia with myositis, or preferably myopathy, since the changes appear to be degenerative rather than inflammatory. Other facts seem to point to the same conclusion, for example : the frequency of Raynaud's symptoms in both conditions ; pain, often referred to as rheumatic in accounts of this type of sclerodermia ; œdema as an initial symptom in both ; the association of " lupus erythematosus " with sclerodermia, quoted by Radcliffe Crocker. The changes in the face and hands in dermatomyositis may be practically identical with those of lupus erythematosus (I remember a case I inherited from Dr. Pernet at the West London Hospital with the diagnosis of sclerodermia, sclerodactylia, lupus erythematosus and Raynaud's disease) ; also the

[1] *Proceedings*, **31**, 1357 (Sect. Derm., 81).

similar distribution of the skin changes in both diseases. Crocker's account also draws attention to the danger of chest complications in sclerodermia. Even the poikiloderma-like changes are mentioned by him as follows: "There may be patchy erythema at first, and later minute vessels are dilated and form telangiectatic tufts and striæ, contrasting with the rest of the surface which, as a whole, is paler than normal. Pigmentation, striated, mottled, or diffuse, is often present over a large area.

Finally, the chief histological alteration in the skin has been sclerosis in every case of dermatomyositis that Dr. Freudenthal and I have had the opportunity of examining, with a single exception, a rapidly fatal case in which only œdema was to be seen.

It would be interesting to know whether symmetrical sclerodermia with sclerodactylia ever occurs without some degree of damage to muscles, and in my experience the complaint of weakness has not often been made voluntarily until it has become very marked.

If this view should prove correct, I believe it would be better to include all cases under one designation, for example myopathic sclerodermia in preference to dermatomyositis, or symmetrical sclerodermia alone should muscular change prove to be constant in that disease.

There is one other point: when the sections were cut, Professor Dudgeon, who examined them, was immediately struck by their close resemblance to the changes that he described in both the skeletal muscles and the extrinsic muscles of the eyeball in Graves' disease (fig. 4).

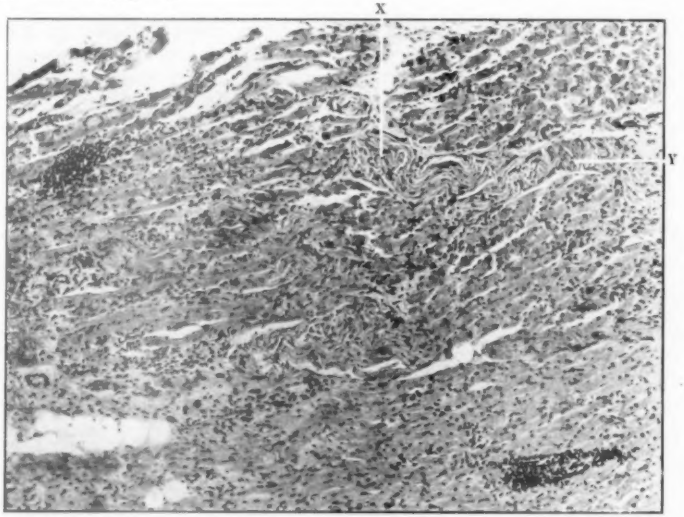


FIG. 4.—Eye muscle from a case of Graves' disease (kindly lent by Dr. J. Bamforth) showing slight muscular degeneration and focal lymphocytic infiltration; in the right upper quadrant tortuosity of some of the muscle bundles (X, Y).

Discussion.—Dr. PARKES WEBER said he had been thinking over the question during the last weeks and admitted that he was coming round to the view put forward by Dr. Dowling, and that such a view represented a great discovery in dermatology. Dr. Dowling had used the phrase "diffuse sclerodermia" meaning one or more diffuse patches, whereas sclerodactylia was a symmetrical diffuse generalized type of sclerodermia, which was what he thought Dr. Dowling really meant.

Dr. A. M. H. GRAY said he had thought at the previous meeting that there was not sufficient evidence before the Section to support Dr. Dowling's contention, but the evidence now brought forward made the association of the two conditions very probable. There were, of course, certain things still to be explained, and it would be wiser to call such cases sclerodermia for the time being, but perhaps later on it would be possible to keep them together in one group. One of the most striking differences seemed to be that sclerodermia cases nearly always started at the periphery, whereas dermatomyositis started on the face. He did not know yet that there was any linking up of the cutaneous changes. Clinically, there was still considerable difference in the two types of lesion, but the association of muscular changes was certainly extremely close. He had no doubt Dr. Dowling would be able to give still further information.

Multiple Epitheliomatosis apparently caused by Arsenic. — H. W. BARBER, F.R.C.P.

Mr. C. L., aged 37.

The patient consulted me a few weeks ago on account of an epithelioma on the lower part of the abdomen.

Examination showed that he had numerous small superficial basal-celled epitheliomata over the trunk, together with hyperkeratosis of the palms and soles.

He had taken arsenic more or less continuously for epilepsy for ten years—1918 to 1928.

Discussion.—Dr. P. B. MUMFORD was not sure that he agreed with Dr. Barber as to the arsenical element in intra-epidermal carcinomata. He had had three male patients with similar disturbances. None of them had taken arsenic. If it had not been for the appearance of the hands of Dr. Barber's patient he personally would not have considered arsenic a provocative factor.

Dr. H. MACCORMAC agreed with Dr. Barber that in many cases of the superficial type of multiple rodent ulcer a history of having taken arsenic for a prolonged period could be obtained. He believed the late Dr. Pringle had first pointed this out.

The PRESIDENT said that some years ago he had shown to the Section a woman who had been taking arsenic and bromide for the prevention of epileptic fits for about twenty years. She had had all the symptoms of chronic arsenical poisoning including numbness of the legs, complete anosmia, a beautiful raindrop pigmentation and multiple keratoses. When he first saw her the palms of the hands, owing to the pronounced arsenical hyperkeratosis, resembled nutmeg graters; however, within a month after the cessation of the arsenic the skin was once more smooth. At that time no epithelioma was present, but subsequently she developed at least one malignant growth on the abdominal wall. He did not think that such cases were particularly rare.

Dr. MUMFORD thought that possibly Dr. Barber and he were talking at cross-purposes. What he had intended to suggest was that multiple intra-epidermal carcinomata were not often arsenical. He agreed that if these were combined with hyperkeratosis the arsenical element should be considered. Multiple lesions of the body of the type seen in Dr. Barber's case were not often arsenical.

Dr. BARBER said that in his experience arsenic seemed to be the provoking factor in many cases of multiple superficial basal-celled epitheliomata, but, of course, not in all cases.

Dr. A. M. H. GRAY agreed that a percentage of such cases had occurred in patients with psoriasis who had been taking arsenic, though a considerable number had not taken arsenic. One saw two types of case, those in which squamous epitheliomata occurred in cases of multiple rodent ulcer (erythematoid benign epithelioma of Graham Little) and those in which isolated squamous or basal-celled epithelioma occurred in patches of psoriasis. Such a case had been described by Whitfield, but others had also been published. The speaker had published a case of a rodent ulcer occurring in a patch of psoriasis in the antral cleft (*Brit. Journ. Derm.*, 1912, **24**, 328).

Three Cases of Mélanose Circonscrite Précancereuse. — H. CORSI, F.R.C.S.

I.—Mrs. M. T., aged 87, has been observed at St. Bartholomew's Hospital for twelve years, on account of a circumscribed pigmentation affecting the right cheek. From time to time a nodule has appeared in the pigmented area. These nodules have been removed, and have been examined microscopically. Histologists have not always been in agreement as to their nature, but looking through all the sections now, there can be little doubt that they were epitheliomata.

The pigmentation varies from pale brown to almost jet-black ; it is scattered in irregular patches on the cheek, but the margins of the patches are fairly abrupt. Close examination shows the pigmented areas to be made up of small dots of varying degrees of brownness. Where there is pigmentation but no nodule, the texture of the skin is unaltered. It has the wrinkled appearance seen in the skin of very old persons, but does not show the characteristics designated as keratosis senilis, or any other alteration except the change in colour. In June 1938 the pigmentation was intense and extensive, and four nodules were present. These were erased under local anæsthesia, and the erased areas treated with three pastilles of X-rays. Seen five weeks later, these places were healed and it was surprising to find that pigment had very largely disappeared, even from areas which had received no X-ray treatment. The patient to-day therefore shows much less pigmentation than is seen in the photograph taken earlier this year.

Nodules have been removed from time to time. These might be recurrences or new areas taking on malignant characteristics. I am inclined to think that, while some may have been recurrences, others at least were new discrete tumours. It seems that any spot in the pigmented area is liable to take on a malignant change, fitting in with Dubreuilh's descriptive term " Mélanose Circonscrite Précancereuse " (*Ann. de Derm.*, 1912, **3**, 129). The condition was first described in 1870 by Jonathan Hutchinson, who called it " Infective Melanotic Freckles " (*Arch. of Surg.*, **3**, 318).

II.—Mrs. L. R., aged 76, has been observed at St. Bartholomew's Hospital for five years. She states that about 1920 a dark spot appeared on the right cheek. This spread gradually in all directions as a dark brown area with almost black spots in it. Excepting the forehead, it now covers almost all the right side of the face. When first seen the pigmentation stopped abruptly just short of the mid-line on the nose and the upper lip. It has extended since then, and has now actually crossed the mid-line (*see* fig.). Five years ago the region about the eye, and the chin were also quite free ; now, both these have been taken into the pigmentary process and show some of the blackest areas. Newly affected patches have usually been blacker than those which have existed for some time.

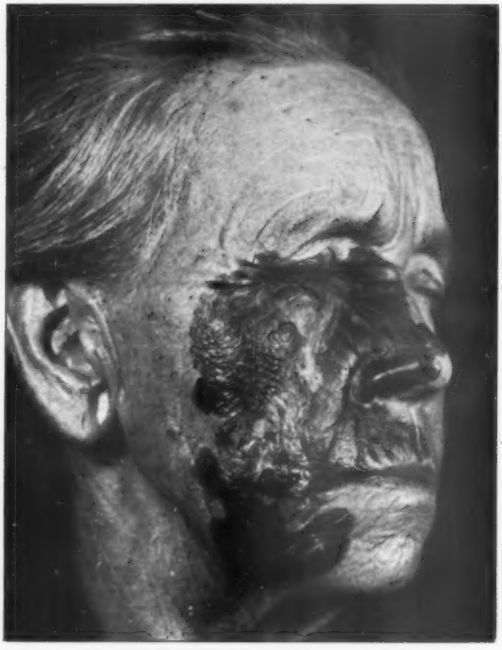
In 1933 a warty growth appeared in the centre and very soon ulcerated. This was treated by the insertion of 4 radon seeds each of 1·1 mc. Section showed pigmented mixed-cell epithelioma. The radon-treated area healed satisfactorily, and now shows relatively little pigmentation. No alteration of texture is noticeable in the pigmented skin, and this accords with the microscopic appearances, viz. a heavily pigmented dermis with thin but otherwise not grossly changed epidermis. Paget cells, however, are present at one end of the section.

III.—E. S., male, aged 47. Two years ago noticed a brown patch on the chin, which gradually got larger and deeper in colour, till it was almost quite black. A few months ago a button-like tumour appeared in the centre. This grew slowly at first, then more quickly, and finally became a nuisance owing to its tendency to bleed. On October 4, 1938, 4 radon seeds were inserted round it. The button itself was erased and submitted for histological examination to Dr. Klaber, who reported that it suggested a malignant melanoma.

In this patient a hard, thick lymph-gland is palpable in the left submaxillary area. No gland enlargement appeared in the previous two cases, and it is possible that even in this patient the enlarged gland can be accounted for by intense buccal sepsis.

As in the previous cases, pigment has tended to disappear following treatment with radon, and the condition is now not readily recognizable.

Histology.—Dr. R. Klaber demonstrated on the screen sections taken from each of the three cases. He said that the histology of this condition was somewhat difficult to interpret. In a section taken from the smooth black surface without tumour formation, the most striking feature at one edge was the presence of large pagetoid cells, which at first might lead one to think that the condition could have something in common with Bowen's disease which often showed vacuolated cells. But further



Case II. Mrs. L. R.

inspection showed pigment in some of these cells which he thought was probably sufficient to indicate that these vacuolated cells were, in fact, malignant melanoblasts. When one came to look at the actual nodules, there were further difficulties. There were masses of pigment and a very loose arrangement of nondescript cells. It was not easy to say whether these were epitheliomatous or melanomatous, but the arrangement of the cells in some areas did suggest close kinship with malignant melanoma.

In a nodule from the second case, the picture was different, but again it was exceedingly difficult to be certain of the diagnosis. It might be a malignant mela-

noma. The histology varied very much. In some parts there was a rather whorled arrangement suggesting some types of transitional or cell carcinoma. Another nodule removed from the same case suggested, on the whole, a malignant melanoma but of rather different structure from the former nodule, shown from the same case. The whorled arrangement of cells was more marked in the latter.

In a section taken from the third case, there was the same picture but with rather more epithelial hyperplasia, and even epithelial islets deep in the cutis, suggesting the possibility that there might be an epitheliomatous component in addition to the melanoma !

Finally, there was a tumour in which the cells showed a very loose reticular arrangement and included pigmented cells which might indicate a malignant melanoma. Again it was difficult to be certain.

He had shown each of the sections obtained to demonstrate the variety of the histological appearances met with in nodules removed from such cases, and to emphasize the difficulty of forming a definite conclusion as to their nature.

Their clinical behaviour appeared to be much more benign than was usual in actively growing nævoid tumours. Their histology was most varied and suggested a greater degree of malignancy than was borne out by their clinical course. The relationship between the different appearances observed in individual nodules was not easily interpreted.

[Postscript.—In the *American Journal of Cancer* (1938, 33, 196), Stout has called attention to " a group of superficial, slow-growing nævo-carcinomas, with Paget-like characteristics which distinguish them from other melanomas ". He refers to papers by Kreibich, Darier, Civatte and Bloch, in which each of these authors has remarked on the close resemblance which may be observed between the Paget cell and an aplastic melanoblast.—R. K.]

Discussion.—Dr. A. C. Roxburgh said that he had " inherited " several of these cases from Dr. Adamson. They did not behave clinically as malignant lesions ; or, if they did, they could be removed before they had done any damage.

At intervals he saw a patient in private who had large areas of black pigmentation on the left cheek. Twice portions of tumour in the centre had been removed and sectioned, but the surgeon had never regarded the growth as being dangerous, and it certainly had never shown any tendency to form metastases. The outlying portions were always improved by electrolysis. In other cases painting the pigmented areas with carbolic acid had been successful.

Dr. I. Muende hesitated to express an opinion on the section thrown on the screen because it was shown for a very short time. He, however, thought the cells which Dr. Klaber described as pagetoid looked more like typical nævus cells, in which case the condition would correspond to that of a pigmented nævus. The first section suggested the early phase in which the pigment cells contained very fine granules and appeared to be segregated before dropping into the dermis.

Pachyonychia Congenita (Jadassohn and Lewandowski). — John Franklin, M.D.

In 1906 Jadassohn and Lewandowski [1] described a condition which up till that time had not been reported, under the title of " pachyonychia congenita " or " keratosis disseminata circumscripta, tylomata and keratosis linguæ ". Their case, a girl aged 15, had a peculiar congenital condition of the nails. All the nails were hard, greatly thickened, and had to be cut with a chisel ; the finger-nails were long and narrow, smooth, shiny, rather transparent, and towards the tips greyish. They were thick at their free ends and curved transversely. The toe-nails were similar and resembled an onychogryphosis. Other symptoms were pointed red papules around the nose and chin. Hyperidrosis of the nose, hands, and soles of the feet ; bullæ

on the soles of the feet ; patches of keratotic follicular papules on the extensor surfaces of the hands and elbows ; keratotic lesions on the palms and soles ; and whitish patches on the tongue. The patient had a brother aged 4 similarly affected.

Since this first case a number of others [2–14] have been reported on the Continent and in the United States under the name of pachyonychia congenita, the essential feature being the curious thickened state of the nails, which is present at or begins very shortly after birth. The other chief lesions which as a rule appear soon after birth, are leucokeratosis of the tongue, symmetrical follicular keratoses affecting the extensor surfaces, keratoses of the palms and soles, and bullæ on the feet. A number of other symptoms have been described, notably hyperidrosis of palms and soles, herpetiform lesions round the mouth, dyskeratosis of the cornea with opacities [13], keratosis of the buccal mucosa as well as the tongue, and in one case involvement of the nasal mucosa and tympanic membranes [2]. The onset of these subsidiary symptoms may take place at any time after birth, sometimes many years later.

The present case :—

O. C., male, aged 17. Machine hand. Out-patient at Westminster Hospital.

History.—According to his mother he was born at the eighth month, when the nails only were affected. At the age of 3 weeks he apparently suffered from a severe stomatitis, which lasted several months. Shortly after this he had some generalized eczematous condition which lasted until about the age of 13 ; this eruption cleared up and was followed by the present horny condition of his skin. In 1923, at the age of 2, he was shown before this Section by Dr. Sequeira as a case of congenital onychogryphosis [15]. No note of any abnormal skin condition was made at that time. There is no history of a similar condition in any member of his family, thirty of whom are known personally to the boy and his parents.

The Registrar's Department of the London Hospital has kindly sent me the following note about him when he was an in-patient under Dr. Sequeira for five weeks at the age of 2 :—

" *History.*—Born with thickened skin in place of nails. One month : Impetigo first on face, now generalized.

On examination.—Solid tubular horny growths from all nail beds ; $\frac{1}{2}$ to $\frac{3}{4}$ in. long ; $\frac{1}{4}$ to $\frac{1}{2}$ in. diameter, projecting at an oblique angle. W.R. negative.

Nails removed under alcohol, chloroform and ether mixture. Patient discharged, having contracted measles."

Present condition.—He is small, well developed, and of normal intellect.

(1) Nails : All nails of both hands and feet are markedly thickened, present a heaped-up appearance, and are a dirty yellow colour (figs. 1 and 2).

(2) Tongue : The tongue is irregularly splashed with smooth white patches which peel off from time to time leaving a shiny red base (leucokeratosis). The buccal mucosa is normal, as also are the teeth.

(3) Skin : This is generally mildly xerodermic with areas of follicular keratosis mainly on the extensor surfaces of the limbs, and on the hips and buttocks where many of the individual lesions are distinctly spiny. On the palms and soles are numerous large discrete keratotic lesions. On the feet, mainly round the toes, there is a tendency to the formation of bullæ which rupture, leaving painful foul-smelling raw areas. On the face there is oily seborrhœa, with comedones and acne lesions. At the angles of the mouth herpetiform lesions which rupture and crust are always present. There are no keratotic lesions on the scalp which is seborrhœic, and the hair is normal. There is no hyperidrosis. There are many deeply pigmented moles on the trunk and limbs.

(4) Eyes : The eyes are normal ; there is no involvement of the cornea.

Wassermann reaction negative.

I think that this is a true case of pachyonychia congenita.

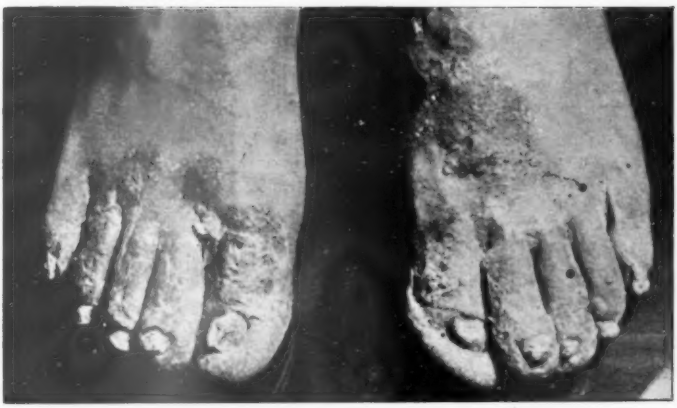


FIG. 1.—O. C.

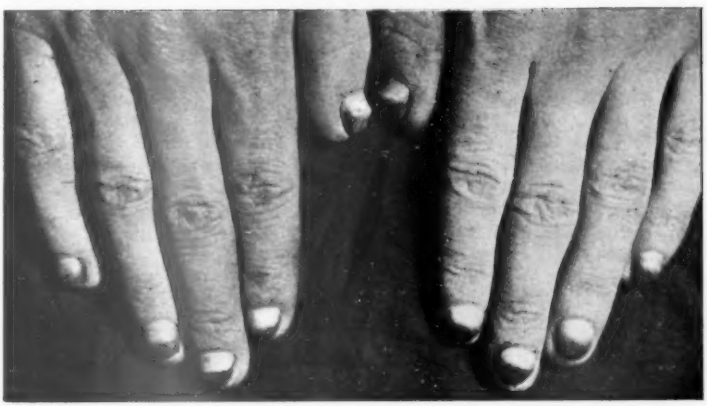


FIG. 2.—O. C.

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16 COCKAYNE, " Inherited Abnormalities of the Skin and its Appendages ". London, 1933 p. 203.
17 PARDO-CASTELLO, " Diseases of the Nails ". London, 1936, p. 151.

Kast's Syndrome (Multiple Hæmangiomata associated with Chondromata or Ollier's Dyschondroplasia).—ALICE CARLETON, M.B., and A. H. T. ROBB-SMITH, M.B. (introduced by Dr. P. C. MALLAM).

E. B., a woman aged 32.

Previous history.—A deformity of the right tibia was noticed in early childhood. At the age of 5 she broke the left humerus, which united badly and slowly. Two hard lumps appeared on the left index finger when she was 10, and the finger was amputated in Newcastle. At 16 or 17, soft lumps appeared on the left leg and foot. These have remained ever since about the same in size and appearance.

Present condition.—There is a diffuse enlargement of the right tibia affecting the lower 3 in., chiefly on the antero-medial aspect. This is tender on pressure but otherwise causes no inconvenience. The left humerus is 1½ in. shorter than the right. A hard tumour can be felt at the distal end of the left index metacarpal. In addition, she has about twenty soft, lobulated, sub-epidermal or subcutaneous angiomata. The epidermis is not involved, and the tumours are softly nodular and in places flaccid. They are nearly all on the left lower limb, but one is on the right side of the abdominal wall. Their size varies from ¼–1½ in. The patient's only complaint is that the tumours "ooze". This is due to a localized but excessive sweating.

Family history.—The patient knows nothing of her paternal antecedents. Her mother is alive and healthy. She has three female children. The eldest has granuloma annulare and signs of past tuberculous adenitis in the neck. The others are healthy.

On examination.—The left foot and ankle are sometimes colder, sometimes hotter than the right. Pearly beads of sweat are seen on the tumours below the knee, but not on those above. Doryl does not affect this sweating. Blood-sugar, blood-urea, blood-calcium, and plasma phosphatase are all normal. The blood-cholesterol is slightly lowered—80 mgm. Wassermann and Meinicke reactions negative. Urine normal.

X-rays show many phleboliths in the subcutaneous tumours, hæmangiomata in the tibia, radius, and humerus, with deformity in the latter. Ecchondromata are seen on the index and thumb metacarpals and the first phalanx of the thumb.

Histological report (A. H. T. Robb-Smith): Biopsies from the following areas have been examined—(1) Nodules from the anterior surface of the right leg: Leiomyomatous hæmangiomata. (2) Nodule from sole of right foot: A simple cavernous hæmangioma. (3) Nodule from back of right hand: Simple cavernous hæmangioma. (4) Subperiosteal nodule from right ankle: Cavernous hæmangioma with calcification of thrombi. (5) Portion of bone from lower end of the left radius: Cancellous bone with an enchondroma.

Comments.—The condition was first described by Kast in 1889. Since then 14 cases have been recorded, of which 12 were male and two female. Seven showed hæmangiomata, chondromata, and Ollier's dyschondroplasia. Five showed a similar picture but without dyschondroplasia. Two showed unilateral hæmangiomata with skeletal atrophy of part of the affected limb. In four instances pigmentary disturbances were also found.

The present case appears to be unique in one feature, the localized sweating and temperature changes. This suggests a link with the angio-neuromyoma or glomus tumour.

Dr. PARKES WEBER said what chiefly interested him was the light the case threw on the condition often termed "congenital varicose veins", an example of which he had described in the *British Journal of Children's Diseases* (1936, **33**, 102), in which there were large giant veins near the right groin. The large veins in Dr. Carleton's case were in connexion with hæmangiomata. He had suggested that so-called "congenital varicose veins" were not in the least allied to what, developing in adults, were ordinarily called varicose veins, but represented a developmental gigantism of certain veins, analogous to the giant blood-vessels in plexiform hæmangiomata.

Darier's Disease.—G. B. MITCHELL HEGGS, M.D., and V. EWING, M.B. (Wing-Cdr. R.A.F.).

Patient, an aircraftsman, aged 20.

Previous history.—No relevant illness.

History of present condition.—Patient noticed rash on face, chest, and back, six months ago. No irritation. Rash then spread to right and left iliac regions of the abdominal wall and upper third of the thighs. No malaise or illness.

On examination.—Greasy, greyish-brown papules on the forehead, cheeks, mid-sternal, and inter-scapular areas of skin. Smaller lesions suggest keratosis pilaris; others are larger and contain a hard plug in the centre. There is a mild degree of pityriasis capitis and some acne vulgaris on the face.

General condition.—Nothing pathological found. No adenitis or splenomegaly.

Tests.—Blood Wassermann reaction negative.

No molluscum bodies in expressed contents of follicle.

Blood-count: Eosinophilia 7½%.

Stools: No worms found.

Dr. I. MUENDE reminded the members that the section shown at the previous meeting had only a few of the features of Darier's disease. It showed the typical form of acanthosis, the plug-like keratinization, and the clefts in the epiderm's, which suggested very strongly the diagnosis of Darier's disease. Since that date he had seen the patient and had noticed that in addition to the lesions on the body he had warty growths on the backs of the hands and minute keratoses on the palms characteristic of the disease. A section was then made from a typical ring-like keratotic lesion on the back, and the histological features in the section shown at this meeting correspond with those found in this disease, that is, the peculiar tongue-like processes coming off the rete pegs, the acantholysis and cleavages in the epidermis, the " corps ronds " and " grains " and the plug-like hyperkeratoses. Although these keratoses have always been described as being follicular, it was the speaker's opinion that this was usually not so, for serial sections of these plugs did not reveal any association with the follicles.

The section was demonstrated, together with palmar prints showing " breakages " in the skin ridges.

Lymphocytoma Miliaris Faciei.—ROBERT KLABER, M.D.

Miss N. K., aged 24, was referred to me by Dr. Stern.

History.—She had epileptic fits from the age of 3 until that of 18, when they ceased. Two years ago she first noticed on both cheeks raised, slightly reddened nodules, which looked like sago grains under the skin. They increased imperceptibly in size and number. There has only recently been some slight irritation and there is no history of light sensitivity. The eruption was first noticed in September 1936 just before her holiday.

On glass-pressure, the nodules were semi-translucent and of pale grey rather than brown colour. It was thought that the condition was either a cystic nævus arising from lymphoid or sweat elements, or possibly a miliary sarcoid of Boeck.

Microscopic section showed only dense localized foci of lymphoid tissue representing each nodule and bearing a close resemblance to normal lymphadenoid tissue (figs. 1 and 2).

Blood-counts on two occasions have shown 14,000 and 8,000 W.B.C.s respectively. In each there was only a very slight increase in the normal proportion of lymphocytes.

Neither spleen nor lymph-glands can be palpated.

The patient appears to be in good health.

Skiagrams of the chest show some apparent increase in hilar shadows. Skiagrams of the feet are negative, but those of the right hand show two small cystic spaces in the right semilunar bone and another in the head of the right 4th middle phalanx.

FIG. 1.—Miss N. K. To show situation in the skin and general structure of a nodule. (× 23·5.)

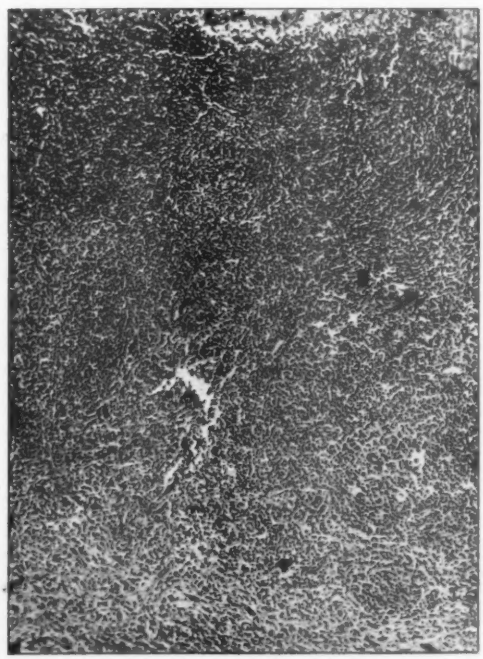


FIG. 2.—Miss N. K. To show darkly staining mature lymphocytes (on left) contrasting with more poorly staining cells (on right) suggesting central germinal follicle. (× 80.)

During the last two months five 100 r doses of unfiltered X-rays have been given to the left cheek. The lesions on this side have now almost entirely disappeared, and those on the right side are much less prominent (fig. 3).

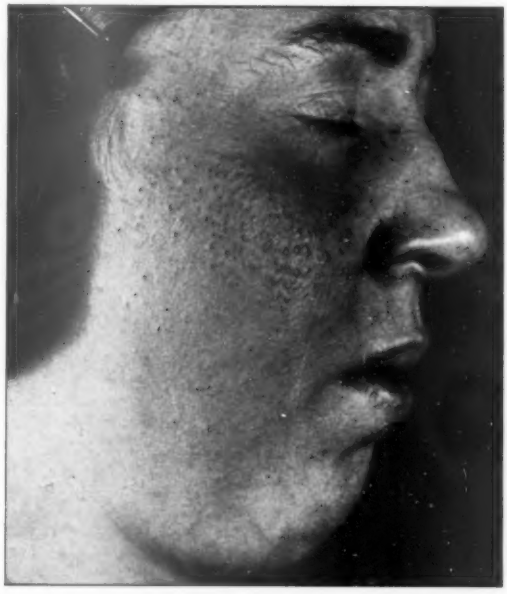


FIG. 3.—Miss N. K. (7.10.38.) Lymphocytoma miliaris faciei.

[POSTSCRIPT (12.1.39).—After receiving two further 100 r doses of X-rays to both cheeks, the nodules have almost entirely disappeared. The patient has recently complained of "seeing black spots" in her left eye, and Mr. Norman Fleming reports that she is suffering from vitreous opacities on this side.—R.K.]

Discussion.—Dr. W. N. GOLDSMITH agreed with Dr. Parkes Weber that the arrangement reminded one of adenoma sebaceum, but the histology was entirely against it. He had seen two cases which he had diagnosed on clinical and histological grounds as lymphocytoma. Neither looked at all like this case. The first had consisted of a few considerably larger lumps on the forehead, resembling Boeck's sarcoid. They had completely and, as far as he knew, permanently disappeared after a few fractional doses of X-rays.

The second had some nodules on the side of the nose. It was interesting that this patient showed in a skiagram a clear space in one of the phalanges. She also had a strongly positive tuberculin reaction. The nodules did not respond to X-rays and began to spread centrifugally and he changed his diagnosis to lupus erythematosus.

Dr. W. FREUDENTHAL suggested that members should read S. Epstein's paper on lymphocytoma (*Archiv für Dermatologie und Syphilis*, 1935, **173**, 181–195) in which he described several cases and also critically reviewed the whole literature and discussed the various possibilities of pathogenesis.

? Benzedrine Eruption.—W. N. GOLDSMITH, M.D.

V. F., female, aged 32.

Present condition.—There are a number of irregularly disposed, flesh-coloured papules on the forehead and cheeks, some of which are excoriated. In the neighbourhood of the lesions the skin has a curious brownish-violet discoloration. The main sensation is pricking. The rest of the skin is normal.

History.—When first seen on April 13, 1938, she had more heavily scabbed sores on the face and scalp, and one little light-red papule. There was some dandruff. She stated that she had had itching papules for at least a year and had the habit of digging at them. She often had cracks inside the nostrils, and some catarrh. The eruption had developed since she began to take benzedrine tablets for narcolepsy. This was the only drug that prevented her from dropping asleep. She found that the spots got worse if she increased the dose and were better if she decreased it. She has been taking no other drugs for any purpose. The dose of benzedrine has recently been reduced but the papules are still appearing.

Treatment.—The nostrils and scalp recovered quite quickly with simple local measures, but the eruption on the face has been entirely uninfluenced by applications. Recently, as she was very anxious for rapid cure, I ordered a few exposures of Grenz-rays. They caused temporary exacerbation and so far there has been no subsequent improvement. The discoloration was present before the exposures.

Comment.—I first made a diagnosis of acné excoriée, but on her second visit I gave up this diagnosis on account of the presence of a number of papules that were not scratched at all and because of the discoloration, which suggested some toxic process. She herself is convinced that it is due to benzedrine.

I am not familiar with a benzedrine rash. Dr. Worster-Drought, who is treating her for narcolepsy, has never seen any cutaneous disorder from benzedrine. We are prevented from testing the matter by stopping the benzedrine entirely as there is no other means of keeping her awake.

Erythrocyanosis Frigida Crurum Puellarum.—W. N. GOLDSMITH, M.D.

M. B., female, aged 16.

Present condition.—Moderate acrocyanosis of hands and feet and face. On a patch of erythrocyanosis on the left leg is a large flaccid blister which has been present about eleven days. There have been others which have burst.

History.—This attack started about three weeks ago. Iodine ointment was applied and caused inflammation and slight vesiculation, but this had subsided under bland ointment before the large blebs formed. She had a similar attack last year also with extensive blistering. There was a large denuded area on the left leg. She also had blisters on the fingers and toes.

Of the investigations the following are of interest: Sedimentation rate: 19 mm. in one hour. Serum calcium 9·8 mgm.%. Tuberculin test: Weakly positive. Skiagram of chest: No active tuberculosis. Basal metabolic rate: +7%.

The sedimentation rate repeated a few days ago is still considerably raised—14 mm. total and 20 mm. maximum.

Comment.—My main reason for showing the case is to illustrate the large flaccid blebs which I have seen in several cases of erythrocyanosis frigida and which seem to me characteristic. I have not seen them described, and Sir Thomas Lewis, to whom I showed this girl, had never met with them. This is the first patient in whom I have seen them on the fingers and toes (last year) as well as on the legs.

Fungating Warts of the Feet.—A. M. H. GRAY, C.B.E., M.D.

S. M., female, aged 16.

History.—The patient first had a small wart on the inner aspect of the right index finger in March 1934. This was followed by a wart on the ball of the left great toe. From this date to September 1934 chiropodists treated the warts by trimming and the application of caustics, but fresh small warts continued to come out on the left foot. In November 1934 she attended the out-patient department at University College Hospital, where the plantar warts were treated with X-rays (1½ pastille dose). When seen six weeks later they had greatly increased in number. She was given

another dose of X-rays (2 pastilles). After another six weeks still more warts had appeared, and some had also appeared on the sole of the right foot. The wart on the hand, which was treated by CO_2, was unaffected by treatment.

In April 1935 she went into the Woolwich Hospital, where the wart on the hand was excised. The left foot was put into plaster, where it remained for fourteen weeks, but after removal the warts were much larger than before. They were then all excised, together with others which had developed on the hands. In spite of this they recurred, and in October 1935 she went to St. John's Hospital, Leicester Square, where she was treated with ionization for about four months, and had one injection of whole blood. The warts, however, did not improve.

In April 1936 she went into a nursing home, where she remained for eight weeks. The warts were first treated by acid, with no effect. They were then scraped under an anæsthetic, but they again recurred.

In June 1936 she went to King's College Hospital, where she was again treated with acids, with little effect. From October 1936 to March 1937 she was in the Sidcup Cottage Hospital, where she was treated with internal medication, belladonna, calcium injections, &c., with no effect.

From March to June 1937 the warts were cut down and treated with acid by a chiropodist, and they now began to get moist and discharge pus for the first time. From October 1937 to September 1938 she was under a homœopathic physician having internal treatment only. During the last year the warts have got larger and discharged pus more freely. She was recently seen at the Radium Institute, where it was thought that the growths were malignant, but no treatment was given.

At the present time the patient is an in-patient in University College Hospital, and presents the following picture :—

The lesions are of three kinds :—

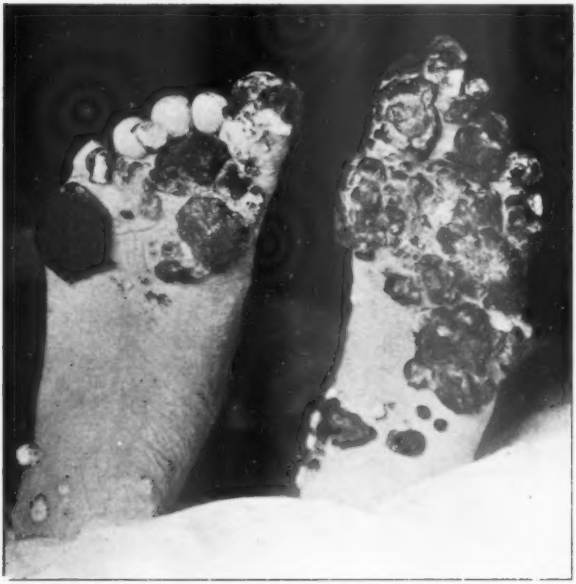
(1) There are a number of ordinary warts with rather thickened and horny tops, scattered over the soles, best seen at the heels. As the patient has not been walking on her feet for some time, these are not depressed below the surface.

(2) Some of the warts show horns growing out of their summit. These are well seen on the tips of the 4th and 5th toes of the right foot, and there is also one present on the tip of the left thumb, and the front of the right index finger, and a very long one on the sole of the left foot.

(3) The most striking lesions, however, are moist, red, granulomatous tumours which occupy the anterior part of both soles, and the undersurface of some of the toes. There are four such tumours on the anterior part of the right foot, one being under the great toe, and a much larger number on the anterior two-thirds of the left foot. These tumours vary from about $\frac{1}{2}$ to $2\frac{1}{2}$ in. in diameter, and some of them are covered with thick masses of sodden horny tissue. The skin has been stained considerably with permanganate of potash (*see* fig.).

The case has been brought to elicit views both as to diagnosis and treatment. I do not think there is sufficient evidence to suggest that the lesions are malignant. There are no signs of enlargement of the glands, although these tumours have been present for some considerable time. They appear to me to be more like infective granulomata occurring on a warty basis.

As regards treatment, I am somewhat reluctant to attempt anything drastic at the moment in view of the numerous attempts that have been made to cure them by surgical means. I am at present keeping her in bed and dressing the feet with 1 : 4,000 perchloride of mercury lotion, and although the treatment has only been applied for a week or so, I think there is no doubt that there is some shrinkage in the larger lesions. I have not done a biopsy, as the patient is in such a highly nervous condition, but I understand that one of the lesions was excised some few months ago, and nothing suggestive of malignancy was found.



Miss S. M. Fungating warts of the feet.

Discussion.—Dr. DOWLING said that some years ago he had once attended an elderly man who had had a plantar wart for many years. This had been treated with X-ray but had persisted; in due course it began to fungate. It was excised and found to be a squamous carcinoma. Shortly after excision it recurred, becoming in due course a large fungating tumour. He died some months later. This was the only occasion on which, in his experience, a plantar wart had become malignant.

Dr. I. MUENDE said that he was of the opinion that the growths were hyperkeratomata rather than hyperacanthomata. If this were the case, the condition might be a hyperkeratotic nævus resembling the case depicted in MacLeod's "Diseases of the Skin", p. 203.

Case for Diagnosis: ? Darier's Disease.—C. H. WHITTLE, M.D.

J. L., a boy aged 6. The eruption has been noted for two months on his forehead and scalp, these being the only parts affected. The lesions are confined to the upper part of the forehead and the frontal part of the scalp extending as far back as the crown of the head, and consist of small pale papules which appear after a short time to have a central black plug and later go on to the formation of quite large papules with crusting. The site of the lesion appears to be in the pilo-sebaceous follicle.

The child is below par in health and has a tendency to colds and coughs.

There is a history of the use of brilliantine for a period of two or three years which has mostly been spread on the front of the scalp. It seems possible that this was acting as a precipitating factor, but not very likely.

[POSTSCRIPT.—The condition has responded well to treatment for acne, and the presumption is therefore that it is a case of precocious acne, probably precipitated by the use of brilliantine.—C. H. W.]

Section of Physical Medicine

President—K. R. Collis Hallowes, M.B.

(*December* 16, 1938)

DISCUSSION ON MANIPULATION IN RHEUMATIC DISORDERS

Dr. A. H. Douthwaite: I propose confining my remarks to the value of manipulation in the treatment of fibrositis, osteo-arthritis, rheumatoid arthritis, and sciatica.

Fibrositis.—Our best immediate and remote results from manipulation are obtained in this group of diseases, provided that the all-important matter of after-treatment be borne in mind. Of the great number of fibrositic areas which might be worthy of mention, I shall deal with three only, namely :—

(1) Chronic cervical fibrositis : This condition vies in frequency with lumbago, and seems to be particularly common among sedentary middle-aged workers, largely no doubt due to the lack of full daily spinal movements which is one of the results of life in cities. The special interest attaching to this is that owing to the close anatomical association between the lesser and greater occipital nerves to the deep fascia of the neck and of the greater occipital nerve to the semi-spinalis capitis and trapezius near their attachment, they become involved in the fibrositic process, with consequent severe pain often at a considerable distance from the morbid process. In short, neuralgic pain radiating over the back of the head, over the temporal region, and occasionally to the supra-orbital area, may be met with. I can offer no explanation for the frontal pain. These individuals have usually been treated for many years with various analgesics without permanent benefit, and help to swell the number of those who have been cured by the osteopath when doctors have failed them. A single manipulation under anæsthesia, followed by deep muscular kneading for several weeks, will usually effect complete cure.

(2) Chronic lumbago : This is a very common condition and one particularly liable to affect the obese middle-aged patient, presumably again for the same reason that he has forgotten how to use his trunk muscles. In such cases manipulation is the first step towards recovery, but will be wasted unless the individual be taught and forced to practise not only spinal exercises, but active abdominal contractions, so as to restore not only his normal suppleness, but also a reasonable girth. Where pain is a troublesome feature, although this seldom is the case after manipulation of chronic lumbosacral fibrositis, considerable benefit may be gained by injecting the erector spinæ on both sides with 20 c.c. of normal saline at three or four points. This should be followed immediately by deep massage.

(3) Scapulo-humeral peri-arthritis : I am considering this under the heading of " fibrositis " because so many of these cases do, in fact, arise apparently as the direct sequel of muscular rheumatism of the shoulder girdle. The salient characteristics presented by a stiff shoulder are well known : the movements are carried out almost, if not completely, by the scapula, severe pain is felt at various points, frequently anteriorly at shoulder level, often at the deltoid insertion, and sometimes radiating down the forearm ; X-ray shows no bony change, but in old-standing cases a line of calcification over the upper part of the capsule may be seen. Muscular wasting is usually present and depends largely upon the duration of the disease. It is this malady which requires carefully graduated and frequently repeated manipulations, although occasionally one finds under anæsthesia that resistance is met at only one point, and when this is overcome the shoulder movement is quite free. It is, however,

of great importance to avoid doing too much at a time, because there is always appreciable post-manipulative pain. Pentothal anæsthesia is adequate for the whole group. In relation to scapulo-humeral peri-arthritis, after-treatment should consist of the induction of muscular relaxation with the application of heat by means of infra-red ray lamp, followed by gentle passive movements for the first day, and subsequently by passive and active movements, the last being the most important, The dull aching pain which is felt in the shoulder after the manipulation, as distinct from acute pain when movement is carried out, can usually be controlled by giving ¼ gr. of codein and 10 gr. of calcium aspirin four-hourly. Usually two or three weeks, sometimes three months, are required to effect a cure, but the ultimate result is completely satisfactory.

Osteo-arthritis.—I have seen manipulation advised as the treatment of osteo-arthritis, but the rationale I am unable to follow. It seems to me that it is impossible to benefit the disease, as such, by these procedures. The problem really resolves itself into whether there is associated fibrositis, and if so, to what extent this is responsible for the symptoms. This varies considerably with different localities. The ordinary osteo-arthritis of the hip is as a rule not benefited appreciably by manipulation, although numerous exceptions can no doubt be quoted. On the other hand, many patients are deprived of the boon of manipulation for a stiff back, because the radiologist has reported that osteo-arthritis of the lumbar spine is present. When we come to examine the films, we find as a rule very moderate osteophytic outgrowths which have been shown to be a normal concomitant of advancing years. In fact the condition is that of osteo-arthrosis. There is seldom any difficulty about deciding these points, because where fibrositis is the important element there is always considerable tenderness to deep pressure over the muscles, and frequently localized and exquisitely tender nodular thickenings can be palpated. I do not, of course, question the value of gentle passive and active movements in the deep water bath, but refer to manipulation under anæsthesia.

Rheumatoid arthritis.—In the acute stage of rheumatoid arthritis, the only manipulation which is justified is that of gentle passive movements of the joints once a day, to prevent as far as possible their becoming fixed. In the chronic stage, where the disease is quiescent, much more can be done. I have noticed that the bogy here is that one may light up a simmering infection. I can only say that I have never seen this happen, and as nobody has yet proved that the joints are actually infected, this fear should be put at rest. With an improved, if not normal, sedimentation rate, normal temperature and pulse and improving general nutrition, one can safely pass on to dealing with the mechanics of the rheumatoid patient. One obtains, I think, the best result from manipulation of the knees and feet and ankles, not only as regards the actual restoration of joint movement itself, but also because it enables the patient to leave his bed and once again to assume the erect posture which is the first sign to him that the end of the disease is really in sight. In no condition is it more important to curb the natural desire to obtain as much movement as possible at one sitting. If this be carried out disaster may occur which may not be only a local one. I once saw the death of a patient from shock within a few hours of an over-enthusiastic manipulation of six stiff joints. Once again, the basal anæsthetics are adequate for the purpose. It is, however, useless to restore movement to joints if there are no muscles to control them ; and as in the chronic rheumatoid we are usually faced with extensive wasting, and a highly deficient circulation as the result of immobility, we must concentrate on this aspect of the disease first, and only manipulate when as the result of massage, static contractions, faradic stimulation, and the application of various forms of heat, the tone and bulk of the muscles are returning. In the upper limbs the shoulders can usually be helped a great deal, but I have never obtained an appreciable improvement in the elbows or wrists, and also the fingers seldom benefit from forced manipulation, but may gradually improve on consistent active exercises, especially against resistance. Once given improved or

correct alignment and strength, we are still faced with the pain which is actually felt in the joint, even though the disease is not active, once the patient stands up. For this reason, I strongly recommend the use of well-made callipers, so that ambulatory treatment can be started as soon as possible. The whole condition of the patient improves so enormously once she starts to walk that everything ought to be done to further this end. The practical difficulty which arises is to obtain light and really well-made callipers at an expense which can be borne by the patient. In a small number of cases where knee-pain in particular has been bad, I have injected local anæsthetics, preferably proctocaine, which has a lasting effect of a day or two, into the joint. This has, however, one drawback, that it interferes with joint sense and thus the balance, but this is not important if the patient is in a calliper because the balance is then dependent largely on sensations coming from the hip-joints which are seldom affected in true rheumatoid arthritis.

Ankylosing spondylitis should never be treated by manipulation.

Sciatica.—Let me say at the outset that I fully realize that the distinction between peripheral and central sciatica is to some extent artificial, and often one meets a mixture of the two. Nevertheless, from the point of view of discussing their treatment, I propose to maintain this division, and first to consider peripheral sciatica or the true sciatic neuritis. Here we have tenderness of the nerve, usually in the buttock and also in the thigh, with loss or profound diminution of ankle-jerk, and some loss of sensation, especially along the outer border of the foot. Stretching of the nerve is painful. In the acute state, of course, no active treatment is desirable, but I am now considering the chronic stage which is seldom reached until at least six weeks after the onset. Whereas most patients with acute sciatica recover completely, if treated properly, a proportion, though free from severe pain, still have some discomfort, especially on movements which involve stretching of the nerve. It is presumed that adhesions are responsible for this; they have formed between the nerve-sheath and the surrounding fascia and muscles, and possibly between the nerve-sheath and the contained fibres. Injection of the nerve with normal saline commonly produces dramatic recovery, and no further therapy is necessary, but in a few stretching of the nerve is also found advisable. When we pass, however, to central sciatica, which we may regard as a sciatic pain almost always due to chronic fibrositis in the lumbosacral region which has resulted in a spread to involvement of the nerves issuing from intervertebral foramina, we have the ideal case for manipulation. It is, therefore, not a true sciatica, but rather an affection of the preplexus components, but the distribution of the pain is frequently the same as that of sciatic neuritis. There is no tenderness of the nerve in the buttock and thigh; the ankle-jerk is usually depressed, but not absent, and loss of sensation, if present, is generally over a much smaller area than the first type. Stretching of the nerve does not give rise to pain. On the other hand, we find the usual tenderness of the muscles of the lumbosacral region, which we associated with lumbago and stiffness of back movements: if forcible flexion is attempted, pain is set up which radiates down the sciatic nerve. Here the combination of manipulation and intrasacral injection of saline produces a high proportion of cures. Once again, after-treatment is important in order to eliminate the reservoir, as it were, of rheumatic toxin. Deep massage, therefore, to the lumbosacral muscles, and active exercises, must be insisted upon. This bears out my earlier remarks that our most satisfactory results from manipulation in rheumatic disorders are to be found in the group which are directly or indirectly referable to chronic fibrositis.

Dr. A. S. Wesson: It is my intention to give my views on the pathological processes which are producing or have produced those conditions benefited by manipulation; and my conception of what such manipulation does towards the re-establishment of normal muscle joint action.

Manipulation is not magic! I would define it as an attempt to maintain, or to

obtain normal freedom of movement in the myo-skeletal system, which has been restricted by some inflammatory process—traumatic, infective, or metabolic—or even by design ; in other words, by therapeutic immobilization.

As a therapeutic measure manipulation is either preventive or corrective, and I am firmly convinced that if we conscientiously maintained the normal full range of movement in all our joints each day ; and if preventive manipulation were the established orthodox treatment of most joint disorders, we should not be here to-night discussing the value of corrective manipulation.

The misinterpretation of Hilton's dictum of Rest for Pain has done as much to retard the treatment of muscle and joint disorders as the misinterpretation of the value of cardiac murmurs did in the treatment of cardiovascular disease before the days of Mackenzie. It is just as important to diagnose a non-tuberculous joint from a tuberculous joint in which rest is indicated, as to diagnose a cardiac murmur associated with a healthy myocardium from a cardiac murmur associated with a diseased myocardium.

In internal medicine it is usually impossible to put the affected organ absolutely at rest, and yet complete recovery may frequently be expected. I believe that such recovery is obtained not because the treatment has *stopped* the normal function of that organ, but because it has *reduced* its work to a minimum.

We cannot stop the heart beating in acute rheumatic carditis, but we can reduce its work by keeping the patient flat in bed. In the same way in the treatment of an acute joint condition we should not stop that joint and its muscles from moving, but we should reduce its work to a minimum.

Our aim in the treatment of acute muscle and joint disorders is to maintain function but to lighten the load. In practice this means :—

(1) The relief from weight bearing ;

(2) Support of the limb from the effects of gravity or imbalance of antagonistic muscles ; and

(3) Manipulation or daily *assisted* active movements of the joint.

Let us now turn to corrective manipulation and think what any manipulation can do anatomically :—

(1) It can stretch or rupture adhesions—intra or extra-articular.

(2) It can reduce a subluxation and regain normal alignment, thereby releasing tension on stretched capsule and ligaments.

(3) It can stretch shortened muscles and fasciæ, whether that shortening be due to spasm or actual contracture.

(1) *The value of manipulation* in the first group has been already clearly defined by Dr. Douthwaite in the treatment of such conditions as he calls scapulohumeral peri-arthritis and in chronic rheumatoid arthritis of knees, feet, and shoulders.

(2) *Reduction of a subluxation.*—It would seem so obvious that a subluxation demands manipulation that it might appear superfluous to mention it here, but when we consider the joints of the vertebral column, how many cases of subluxation are diagnosed as acute rheumatic processes, stiff neck, pleurodynia, lumbago, &c. ?

The clinical picture of sudden onset of pain and loss of function, local tenderness and deformity, is attributed to muscle spasm, but in many cases the muscle spasm obscures its underlying cause—namely a subluxation of a vertebral joint. I admit that those patients who are deprived of the benefit of our manipulation—or more possibly, frequently, that of an osteopath—will often recover spontaneously with or without the assistance of heat, massage, Sloan's liniment, or Fynnon's salts. But what of their future ?

Adaptation to the changed alignment occurs with freedom from symptoms. Acute exacerbation may occur from trauma of comparative mildness, but eventually chronic symptoms arise not only from the originally affected joints but from other joints and muscles whose use has been irregularized as the result of abnormal transmission of force.

An X-ray at this stage, years after the original damage, reveals osteo-arthritic change. I ask you, should this be termed a disease process? Or should we not, more rightly, ascribe the bony changes to abnormality in function over preceding years? If you agree, then surely we should insist on manipulation to prevent these otherwise inevitable pathological changes.

In practice, the best results in this type are obtained by a single manipulation under anæsthesia, followed as quickly as possible by maintenance of mobility by assisted movements. Only those who have had the advantage of seeing and using under-water manipulation will appreciate its inestimable value. I have had installed at my hospital a tank of such dimensions that full movements of the arms, legs, and trunk, can be obtained under water, with the assistance of a masseur, Dr. Hugh Burt, or myself.

(3) *Stretching of shortened muscles or fasciæ.*—Lastly, I wish to discuss a very large group of cases in which there is no history of acute injury and no acute or catastrophic onset of pain; but there has been an insidious onset and unrelenting course of aching pain, either in neck, shoulder and arm, or back, buttock and leg—labelled for want of exact knowledge of its pathology—brachial neuritis, chronic lumbago, or sciatica.

Examination reveals tenderness in certain muscle groups, pain on certain movements, deformity, and, if of long standing, osteo-arthritis of underlying vertebral joints. Here again, in my opinion, the bony changes are entirely the result of limitation of normal mobility, but this time the result *not* of sudden injury but of chronic malposture.

If a joint is held fixed for any length of time in such a way that its full range of movement is limited, then the muscles moving that joint will show certain characteristic changes. On the concave side there will be shortening and contracture both of muscle-fibres and fasciæ, and on the convex side, lengthening and atrophy, which are clearly seen in simple hinge-joints such as the knee.

When we turn to the spinal joints the habitual maintenance of any abnormal posture must produce the same effects, and I will illustrate three types of malposture pointing out those muscle groups and underlying joints which must necessarily be subjected to pathological stresses and strain.

In the first type the outstanding abnormality is an increased lordosis accompanied by an increased downward inclination of the anterior pelvis, and persistent slight hip flexion. Applying the principles of muscle balance as enunciated above, to the lumbar and pelvic joints, let us imagine them to be two simple hinge-joints. The increased extension of the lumbar spine will give rise to lengthening and weakness of the flexors, viz. rectus abdominis, and shortening and hypertrophy of the erector spinæ muscles. Conversely the hip extensor, gluteus maximus, will be lengthened and weakened, whilst the hip flexor (ilio psoas) will be shorter and stronger.

In addition we see in fig. 2, which represents this type diagrammatically, that there is an abnormal transference of the body-weight as represented by the vertical line through the ankle-joints (cf. fig. 1), resulting in a considerably increased load on the lower erector spinæ muscles. Clinically, this excessive postural load will lead first to fatigue pain, but later to persistent low backache, the result of structural changes in the muscles, fasciæ, and intervertebral joints.

Exactly similar pathological changes and clinical symptoms will be found in the neck, when a cervical lordosis is present.

The aim in the treatment of this type is to realign the lumbar spine, pelvis, and hip-joints. In the early stages this can be done entirely by exercises, the basic one being a simultaneous contraction of the abdominal and gluteal muscles. When this is carried out correctly the pelvis is extended on the femora, till its inclination is normal, and the abnormal lumbar curve disappears. At the same time the body-weights will become more evenly balanced, as can be shown by examination of the patient with a plumb line.

In the later stages when there is a fixed contracture of the muscles of the lower back, with loss of mobility in the vertebral joints, a forcible flexion manipulation under anæsthesia is essential before remedial exercises are instituted.

Let us look briefly at the other two common types of malposture. Fig. 3 illustrates that most frequently seen in males, and might be termed the " fire-place " attitude. Here the hips are fully extended, and the body-weight is borne on the strong anterior ligaments of the hip-joint, the pelvis is almost horizontal, and the lower back is flat.

In this type there will be shortening of the glutei and hamstring muscles and their fascia. The effect of this shortening is frequently brought to light by occupations in which considerable effort has to be used when the spine and hips are flexed and the knees extended, e.g. heavy weight-lifting, digging, and lorry driving. Owing to the shortening of the glutei and hamstrings strain falls excessively on the sacro-iliac joint and its ligaments, resulting in low back and sciatic pain.

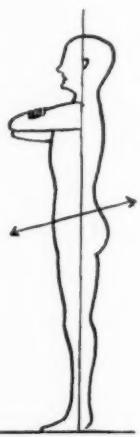


FIG. 1.—Normal posture.

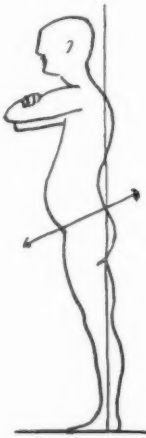


FIG. 2.—Lordosis and forward posture

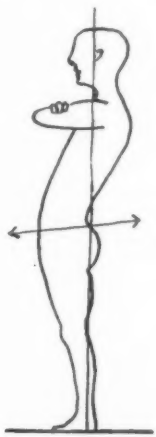


FIG. 3.—Male type. Backward posture.

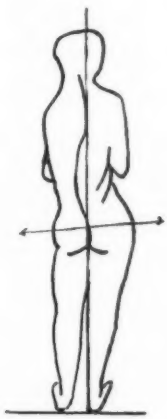


FIG. 4.—" Shop-girl's " hip.

In this group, manipulation of the affected sacro-iliac and stretching of the shortened muscles is the first step in the treatment.

Lastly, fig. 4 represents a posture frequently seen in girls whose occupation demands long hours of standing, and has been described as " shop-girl's hip ". The leg upon which the weight rests is held locked in adduction. The pelvis is rotated, and there is a secondary postural scoliosis. Backache, and sciatic pain referred from the hip abductors and rotators is the clinical picture, and a positive Trendelenburg's sign can usually be elicited. Here manipulation of the lumbar spine may be necessary as well as exercises designed to strengthen the weakened hip muscles.

In all these groups the primary pathological change occurs in the muscles, and in the earlier stages of clinical disability a return to normal function can be expected by remedial exercise or auto-manipulation ; but in long-standing cases, so much contracture has taken place in the non-expansile elements of the muscles or in the capsules and ligaments of the underlying joints, that forcible manipulation is the essential foundation on which we can rebuild—architecturally and mechanically—a well-balanced, efficient, and erect animal.

Section of Orthopædics

President—R. OLLERENSHAW, F.R.C.S.

[*October* 4, 1938]

Multiple Epiphyseal Dysplasia.—PHILIP WILES, F.R.C.S.

J. P., female, aged 6 years.

Personal history.—It was noticed, when she was an infant, that her fingers would not bend properly. Treated at a welfare clinic by forced movement, without improvement. Has recently complained of pain in the left knee.

Family history.—No consanguinity. Siblings: Female 1 year; female 4 years (by second husband). Patient aged 6 years (by first husband). The mother says that no similar disorders were known amongst relatives.

On examination.—Small child for age. Forearms: Short and broad at elbows. Hands: Short stubby fingers. Flexion at metacarpo-phalangeal joints very limited.

FIG. 1.—J. P.

FIG. 2.—J. P.

FIG. 3.—J. P.

FIG. 4.—J. P.

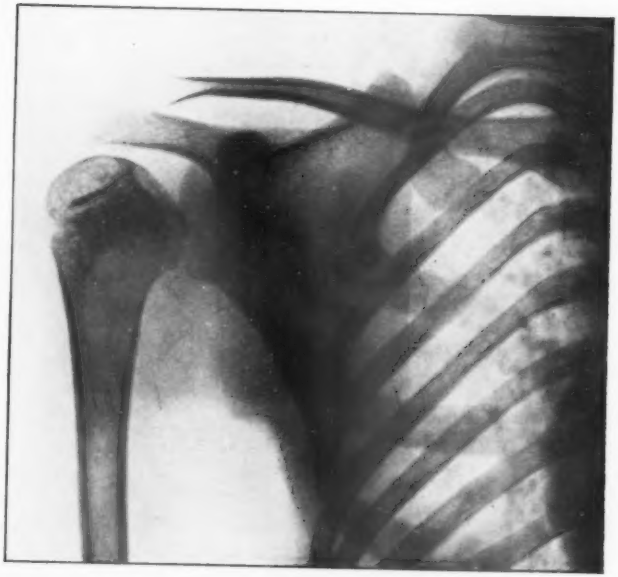


FIG. 5.—J. P.

Knees: Both internal condyles of femora prominent. Left knee: Extension limited about ten degrees; marked valgus, which has increased during the last month.

Skiagrams: All the abnormalities are bilateral and symmetrical. Changes of the type of osteochondritis in the following joints: Humerus, proximal and distal epiphyses; radius, distal epiphysis; femur, proximal epiphysis.

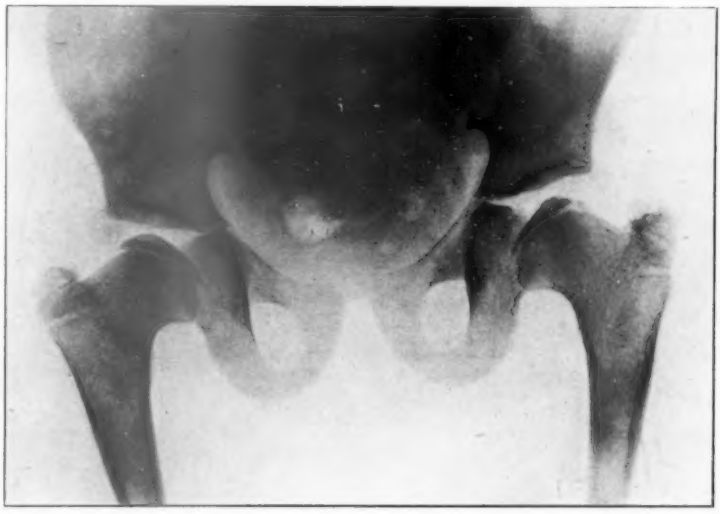


FIG. 6.—J. P.

The epiphyses of all the metacarpals and the proximal phalanges of all fingers and toes are abnormal. There is delay in appearance of the lower ulnar and upper radial epiphyses.

The following cases were also shown:—

I.—Occupational Arthritis of Carpo-metacarpal Joints.

II.—Coxa vara.—J. S. BATCHELOR, F.R.C.S.

Spondylolisthesis (Report of a Case, with Skiagrams).—G. O. TIPPETT, F.R.C.S.

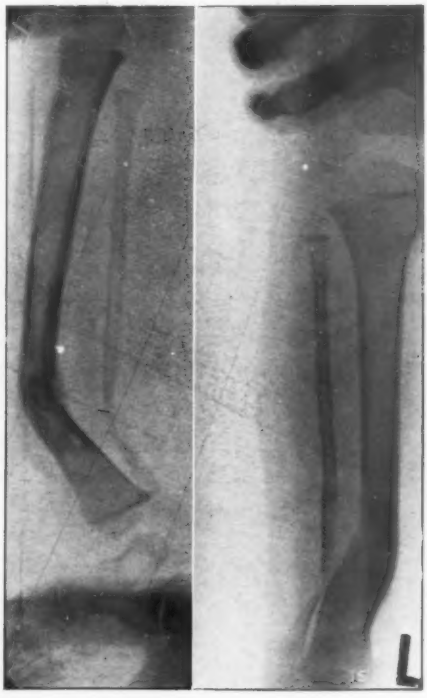
Some Recent Cases of Spondylolisthesis (Skiagrams).—NORMAN CAPENER, F.R.C.S.

Demonstration of a Modification of the Atkinson Range-Finder.—RALPH BROOKE, F.R.C.S.

[*November* 1, 1938]

Malunion of Tibia and Fibula.—W. HARVEY GERVIS, F.R.C.S.

Boy aged 2 years 3 months, first seen by me a few weeks ago with a fracture of the tibia and fibula at the junction of middle and lower thirds. The tibia is apparently firmly united with much angulation. The fibula is much attenuated at site of fracture and not united. The child will not walk.



15.10.38. Boy: 2 years 3 months.

History.—Fractured tibia and fibula at the age of 3 months. Was not treated for six months, then had various treatments at different institutions. During that time the bones never united, and the child never walked. Finally, in Scotland, a plaster was put on, and the patient subsequently moved to Tunbridge Wells. When the plaster was removed two months ago the bones had united, but there is much angulation and the fibula is much attenuated at the site of fracture.

Albers-Schönberg Disease.—A. T. FRIPP, F.R.C.S.

K. F., female, aged 13 years.

Family history.—Mother and father alive and well. Two sisters. One aged 20 years has no symptoms, but she has not been X-rayed. One aged 8 years; skiagrams of bones normal.

Previous history.—1.10.37: Fracture of left femur at junction of upper and middle thirds. Convalescence was uneventful and the fracture united in good position. On

re-examining the skiagrams taken at that time, it is clear that the condition was present in the lower end of the left femur at the time of the accident, but the texture of the bone at the site of the fracture was normal. The bone changes appear only in the extreme lower margin of the films and I did not appreciate their significance at that time.

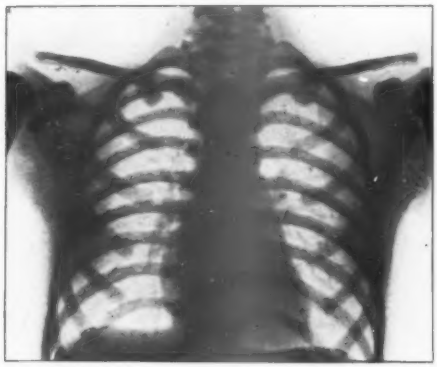


FIG. 1.

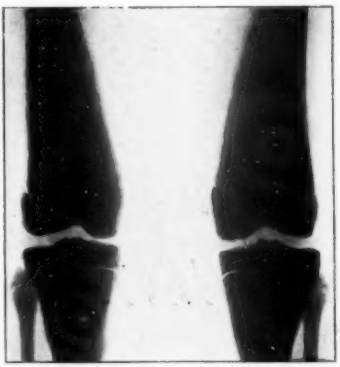


FIG. 2.

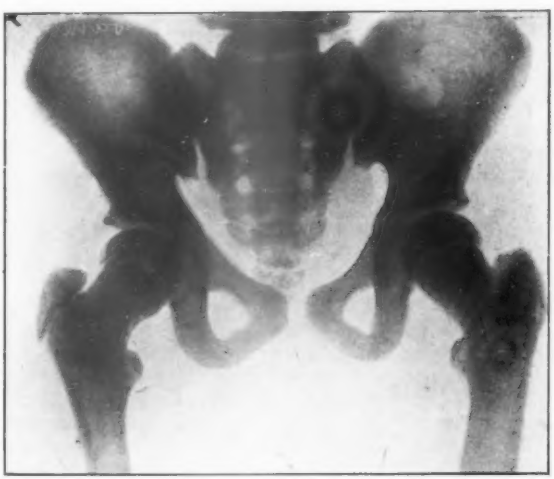


FIG. 3.

FIG. 4.

K. F. September 1938.

In September 1938 the girl complained of aching in both knees and was again brought to hospital.

On examination.—A healthy-looking well-built girl with no obvious anæmia. There is thickening of the lower end of both femora and upper ends of both tibiæ. Flexion of both knees is slightly restricted. Vision is normal and there is no optic

atrophy. X-rays show changes typical of Albers-Schönberg disease in the pelvis; upper and lower ends of both femora with a normal area in the shafts; upper ends of both tibiæ; vertebræ; ribs; upper end of left humerus. The X-rays show increased density with transverse striation and broadening of the affected parts of the long bones.

Blood-count: R.B.C. 4,760,000; Hb. 94%; W.B.C. 13,500.

Serum calcium 10·8 mgm. per 100 c.c. Serum inorganic phosphate 4·11 mgm. per 100 c.c. Plasma phosphatase 0·29 units.

Discussion.—Mr. H. A. T. FAIRBANK: Anæmia is often a marked feature of these cases and leads to fatal results, although one can get bone changes without the anæmia and I myself have known a patient who lived to 70. I am under the impression that the mortality is proportional to the fibrosis of the marrow; optic neuritis is not uncommon, and in all my cases I found the phosphatase to be normal.

Mr. OLLERENSHAW pointed out the association of deafness with this condition.

Multiple Deformities in Two Sisters.—St. J. D. BUXTON, F.R.C.S.

These two girls are highly intelligent and great friends. The facial appearance is identical. The face is flat with sunken nose; the nostrils are patent. The palate is high, teeth notched but enamel well formed. There are no peg-shaped teeth. The facies appear more like those of achondroplasia than congenital syphilis.

The limbs are probably in correct proportion to the trunk. The hands show rather bulbous ends to fingers, thumbs and toes, which may be "clubbing". In both children there is an epiphysis at each end of the 2nd metacarpal bone, the proximal one being irregular in ossification.

Phyllis W., aged 10 years, has scoliosis, medial subluxation of both elbow-joints with deformity of epiphyses, dislocation of both hips, anterior dislocation of both knees. Right os calcis deformed. Syndactyly of two toes. Right foot has high arch with equinus deformity. Her strange mode of progression is due to 90° of hyperextension at each knee. Wassermann reaction positive. Meinicke reaction positive. Serum calcium 9·9 mgm.%; phosphatase 23·4 units % (normal 5–15 units %).

Maisie W., aged 9 years, has subluxation of the elbows like her sister and bilateral uncorrected talipes equinovarus. Wassermann reaction negative. Meinicke reaction positive. Serum calcium 9·8 mgm. %; phosphatase 22·5 units %.

Family history.—The father is reputed to be small and deformed, but the mother has a normal appearance. Since these two girls were demonstrated the brother, aged 18 months, has been examined. His facial appearance is similar to that of the girls. He has scoliosis, lateral subluxation of the elbows; there is a dislocation of the right hip-joint and anterior dislocation of the right knee, both similar to those of Phyllis, but there is only 30° of movement at the knee, most of this being hyperextension. There is a severe equinovarus deformity of the left foot similar to that of Maisie. His Wassermann reaction was negative.

Mr. KENNETH HERITAGE wished to remark on the excellent results which often follow prompt reduction of the commoner type of congenital bilateral anterior subluxation of the knees. Such a case has been watched for the past six years; growth has proceeded normally and the knees are completely normal, although when first seen a few days after birth, a condition of rigidly locked hyperextension was present. X-ray examination showed anterior displacement of the tibiæ on the femora. Reduction under anæsthesia was carried out without difficulty and fixation in flexion maintained for a few weeks.

FIG. 2.—Profile of Phyllis. (26.10.38.) She walks in this position using a short stick.

FIG. 1.—General aspect of girls. Phyllis is balancing on her legs, with knees hyperextended, and Maisie standing in position typical of untreated talipes equinovarus. The deformity of the four elbows is evident.

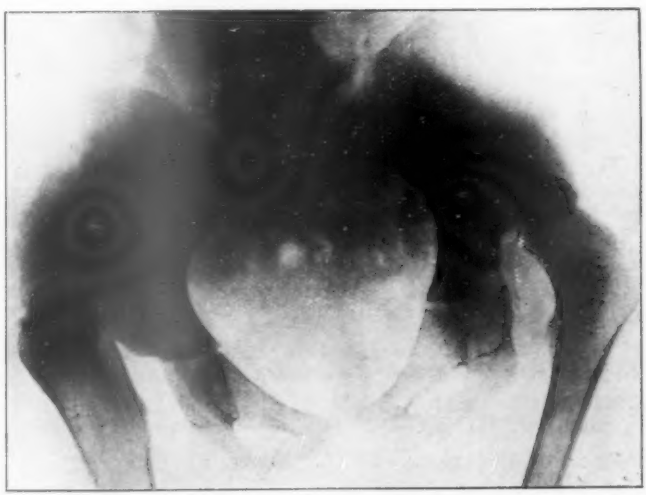


FIG. 3.—Antero-posterior view of skiagram of pelvis of Phyllis. Neither femoral head is in the acetabulum, and each is on the dorsum ilii. The left femoral neck is shown to be more solid than in the average case of congenital dislocation of the hip.

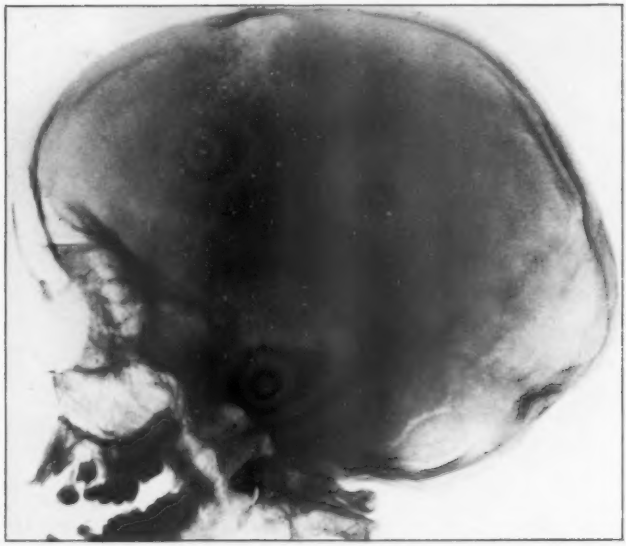


FIG. 4.—Lateral view of skiagram of skull of Phyllis. The sunken nose and so flattening of the whole of face is shown. The pituitary fossa is small.

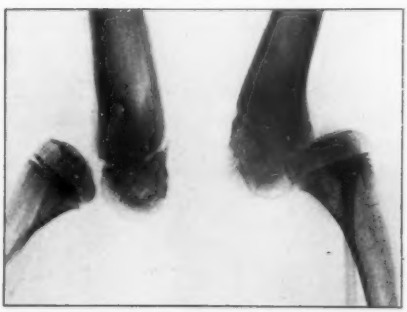


FIG. 5.—Lateral view of skiagram of both knees of Phyllis. The tibia is displaced forwards and upwards. The lower end of the femur is abnormal in shape. Texture of bone and epiphysis is normal.

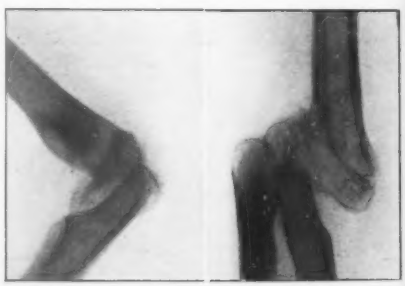


FIG. 6.—Skiagram of Phyllis' left elbow. The lateral view shows the absence of the forward angle at the lower end of the humerus, and backward dislocation of the upper end of the radius, the epiphysis of which is normal. The antero-posterior shows medial dislocation with the deformity of the lower end of the humerus.

The following cases were also shown :—

Syphilitic Osteitis with ? Bilateral Charcot's Disease of Hip-Joints.—J. C. NICHOLSON, F.R.C.S.

Kyphosis : For Diagnosis.—G. O. TIPPETT, F.R.C.S.

Anterior Poliomyelitis.—J. A. CHOLMELEY, F.R.C.S.

ERRATA

"PROCEEDINGS", 1938, 32 (Section of Obstetrics and Gynæcology).

Page 1. After author's name, W. E. Caldwell, *for* "F.C.A.S." *read* "F.A.C.S."

Page 10. Fig. 5, legend B. "The method of engagement illustrated in fig. 5 A takes place along the axis of the curved area", *for* "area" *read* "arrow".

Page 28. Reference 16, *for* "Barnes, J. M. . . ." *read* "Barnes, Robert, 'Lectures on Obstetric Operations', London, 1870. J. Churchill & Sons, p. 68."

Section of Obstetrics and Gynæcology

President—ALECK W. BOURNE, F.R.C.S.

[*November* 18, 1938]

Further Studies in Adult Rickets (Osteomalacia) and Fœtal Rickets

By J. PRESTON MAXWELL, M.D., F.R.C.S., F.C.O.G.; H. T. PI, M.D.; HAZEL A. C. LIN, A.B., M.D.; and C. C. KUO, M.D.

(From the Department of Obstetrics and Gynecology and Ophthalmology, Peiping Union Medical College)

IN 1934 details of two osteomalacic pelves from China were given [1]. One of these came from a woman, a three para, who was aged 39, and in whom the active process was healed. The second was also from a multipara, aged 43, a six para in whom the disease was still active. We now add the details of a third specimen in which our previous work has again been confirmed, showing the close connexion which exists between late rickets, adult rickets, and fœtal rickets (figs. 1 and 2).

This pelvis is from a primipara in whom the disease was still active, and in whom, as an adolescent, the characteristics of a fully developed osteomalacic pelvis were already present. The fœtus also showed fœtal rickets.

Mrs. C. W. H., aged 18, a prostitute, Chinese, came to the Peiping Union Medical College Hospital on February 15, 1936. Her last monthly period was on June 12, 1935, and her expected date was therefore March 22, 1936. Labour pains had started on February 12, 1936, and she had been examined by an old-type midwife on February 13. After a very severe pain on February 14, labour pains had ceased, and the parts of the fœtus were clearly felt in the epigastrium.

She was in a state of collapse, with dyspnœa, and a hardly perceptible pulse. Free gas was present in the abdominal cavity.

Under local anæsthesia the abdomen was opened and a true Porro's operation was done, and the fœtus, placenta, and uterus removed, much free blood being found in the abdomen. The uterus had ruptured across the front of the cervix, well out into the left broad ligament, and the shoulder of the fœtus was caught in the rent. Gas was present in the broad ligament tissue.

She rallied somewhat, but in spite of transfusion, and glucose and saline, died seven hours later. Her pelvic measurements were as follows: Interspinous, 20 cm.; intercristal, 23 cm.; ext. conjugate, 18 cm.; interischial, 3 cm.; posterior sagittal, 8·5 cm.

For the previous three years, i.e. since the age of 15, she had complained of aching in the back and legs; and, for the last two years, the standing height had been noticeably diminishing. She was much dehydrated.

Blood-count: R.B.C. 4,650,000; Hb. 15·4 grm.; W.B.C. 6,850.

Blood-calcium, 8·56 mgm. per 100 c.c. of serum
Phosphorus 2·2 mgm. per 100 c.c. of serum } (in spite of the dehydration).

Blood Wassermann positive.

A skiagram showed osteomalacia with a triradiate pelvis. The fœtus showed the signs of fœtal rickets. Its development corresponded to the thirty-fifth week of pregnancy. Its weight was 2,200 grm.

One interesting feature of the case is the age of the mother, and another is the clear signs of fœtal rickets at the 35th week of pregnancy.

Finally, to settle, from the clinical point of view, the question of the relation of adult to fœtal rickets, the following case, which we have carefully followed, presents features which fill in some of the lacunæ in our previous publications.

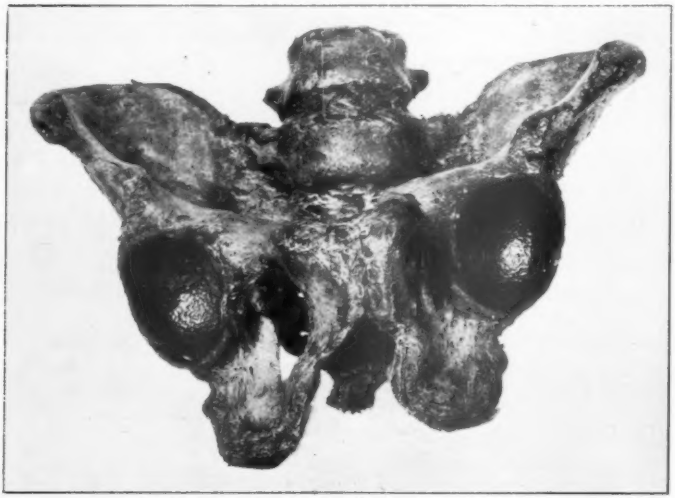


Fig. 1.

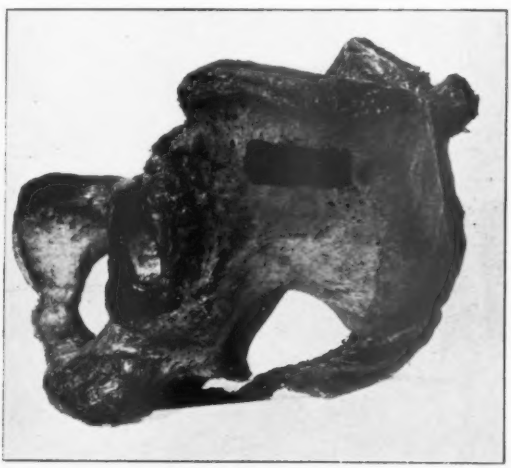


Fig. 2.

Mrs. T. L. F., aged 23, a Chinese housewife, came to the Obstetric Clinic of the Peiping Union Medical College on October 5, 1934, with a six-months' pregnancy. She was found to have a 4-plus-Wassermann reaction, was referred to the Syphilis Clinic, was properly treated with

neoarsphenamine, and without untoward reaction. The child, her third, was born at home at term and lived, but developed rickets.

She dropped out of sight, and on her next visit was admitted to hospital at or near term, on April 30, 1936. She was œdematous and had been suffering from tetany on and off for six months. Her history in detail was as follows :—

She had occasionally suffered from back and thigh pains since the age of 14, especially in the winter, with occasional numbness of the extremities. Her diet had consisted of white rice, wheat flour, and vegetables ; rarely meat, eggs, or animal fat.

She had had three children, the first did not walk till 4 years of age and had bent legs ; the second died of vomiting at the age of 40 days ; the third did not walk till 2 years of age and has bowlegs.

The patient had some albumin in her urine, but her blood-pressure was only 100 systolic, over 80 diastolic. She was spontaneously delivered of a living female baby weighing 2,450 grm., with marked fœtal rickets.

Her Wassermann and Kahn reactions were faintly positive ; the baby, however, showed no signs of syphilis, nor has she subsequently developed any sign of this disease.

On admission her blood-calcium was 4·0 mgm. per 100 c.c. of serum, and the blood-phosphorus was 2·6 mgm. per 100 c.c. of serum. She was at once placed on calcium and calciferol. The course as regards her blood picture was as follows :—

April 30	Ca 4·0 per 100 c.c. of serum P 2·6		May 18	Ca 9·75 per 100 c.c. of serum P 6·15	
May 7	Ca 5·62 „ „ „ „ P 3·88		May 23	Ca 9·20 „ „ „ „ P 5·48	
May 11	Ca 8·4 „ „ „ „ P 5·0		June 1	Ca 8·9 „ „ „ „ P 4·0	

She left hospital well, the urine showing no abnormality.

Her blood hæmoglobin on entering hospital was 8·1 grm.%, and on discharge 10·8 grm.%. One of the interesting things about the case was the pelvic measurements. In 1934 these were as follows : Interspinous, 22 cm. ; intercristal, 26 cm. ; ext. conjugate, 19 cm. ; interischial, 10·5 cm. Arch wide.

By the time of her admission the interischial diameter was down to 8·5 cm., her pubic arch was narrowing, and there was no doubt that pelvic contraction was beginning. The remaining measurements were as before noted.

To turn to the child. At birth on April 30 it weighed 2,450 grm. and its height was 32/47 cm. Its cord blood contained only 6·4 mgm. calcium and 4·2 mgm. of phosphorus per 100 c.c. of serum. The Kline, Wassermann, and Kahn tests, were negative.

On May 9 definite carpopedal spasm, and spasm of the face, were noticed. On May 11 the blood-calcium was up to 7·46 mgm., and by June 25 it had risen to 11·95 mgm.

The X-rays showed marked fœtal rickets, and the bone shadows were very poor. At birth the limbs were normal. On May 2, about forty hours after birth, in spite of special handling, the left femur was found fractured at about the middle of the shaft. Some time between May 10 and 20, in spite of still further care in handling, the right femur was fractured near its lower end. On May 21 a fracture was also noticed at the junction of the upper and middle thirds of the right ulna.

By June 15, 1936, the fractures were apparently healed.

Treatment was by a formula of glucose and breast milk, with orange juice 10 c.c. three times a day, and 5 drops of haliverol twice a day.

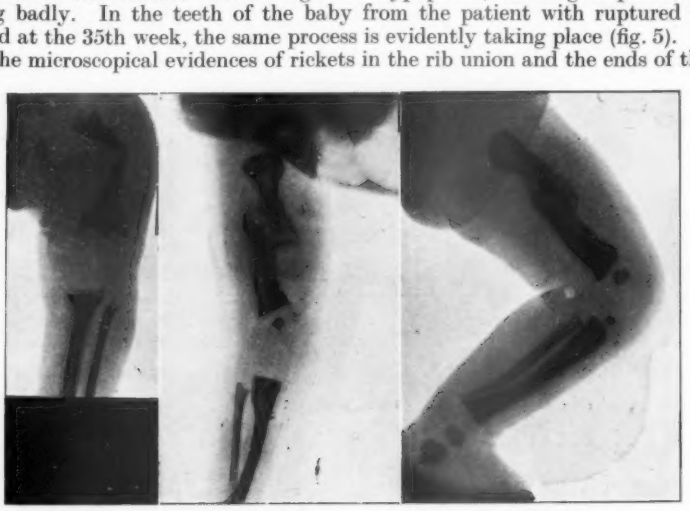
The child was slow in crawling, and in attempts to sit up. The first teeth, the lower central incisors, came through at about 1 year and 2 months. She did not walk till 2 years and 2 months of age.

One of the most remarkable things about the case was the healing of the fractures with the gradual obliteration of deformity (figs. 3 and 4).

In the mother, there are some signs of late rickets and mild adult rickets ; two of the children exhibited infantile rickets, and the last baby had marked fœtal rickets.

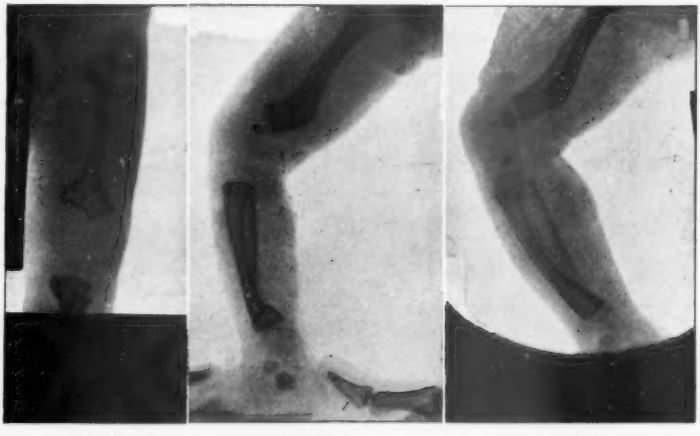
In our last paper [1] we described the changes which take place in the teeth of

children born with the evidence of fœtal rickets, and pointed out that in addition to other defects the enamel showed signs of hypoplasia, forming imperfectly, and staining badly. In the teeth of the baby from the patient with ruptured uterus, removed at the 35th week, the same process is evidently taking place (fig. 5). In this fœtus the microscopical evidences of rickets in the rib union and the ends of the long



3.5.36. 22.5.36. 15.6.36.

Fig. 3.—Baby T'ièn. Left femur. (Bone shadows have been intensified).



2.5.36. 23.5.36. 16.6.36.

Fig. 4.—Baby T'ièn. Right femur. (Bone shadows have been intensified).

bones are typical. In a good many of our Chinese cases the formation of osteoid is not marked, and this is probably due to the general malnutrition.

We have already written fully on the question of posture in the production of the typical triradiate deformity of the osteomalacic pelvis, and in the formation of the flat pelvis which one finds as the result of infantile rickets [1, 2]. Where a patient who

is developing an osteomalacic pelvis sits all day, she gets a fairly even, triradiate deformity. If, on the other hand, she lies mainly on one side, there is an irregular triradiate pelvis with the side on which the patient lies pressed in more than on the other side. These are severe well-marked deformities, but it is as well to remember that there are many modifications of the normal pelvis caused by mild rickets, which approximate closely to the forms of pelvis described by Caldwell and Moloy [2], the genesis of which is as yet somewhat obscure. A mild form of flat pelvis approximates very nearly to the so-called "platypelloid" type, whilst pressure resulting in a moderate yielding at the two sides will produce a pelvis which is, in all essentials, of the "android" type. Thoms [3] has already put forward the possibility of a

Fig. 5.—Baby C. W. H. Tooth showing enamel change. (×110).

"gynecoid" type being due to mild rickets. Undoubtedly there is a congenital element, possibly also a hormonal one, in the formation of the adult pelvis; and the anthropoid type may be of this nature. But in our opinion mild rickets plays a much larger share in the final shape of the adult pelvis than has been conceded in the past.

In a previous paper [4] the question of instability of gait of patients in late pregnancy has been mentioned. It is a moot point whether in the vast majority of cases relaxation of the pelvic joints with instability of gait is not due to a mild degree of vitamin-D deficiency. We have never been able to satisfy ourselves that such was not the case, as we have seen the condition clear up before labour under calcium and vitamin-D treatment; and mild conditions of this deficiency disease are by no means uncommon.

There is a further interesting fact to be noted about these cases of osteomalacia

with osteoporosis. The symphysis pubis is apt to be weakened, and unless special care is taken, may give way during delivery. We have known this to happen on several occasions, and the force needed is very slight. On one occasion Maxwell had this experience whilst doing a perfectly easy low forceps delivery in a mild case of osteomalacia, pulling with only one hand. As a rule this separation seems to take

Fig. 6.—Sitting posture of Shansi woman

place rather than fracture of the pubic rami, though where a funnel pelvis has been produced, and has been unrecognized, the disease being healed at the time of delivery, splintering of the pubic arch may occur [5].

One of the conditions modifying these deformities in North China is the posture so many women adopt when sitting on the "K'ang" (a hot platform), in their homes. When one puts one of these women into a lithotomy position, one finds an unusual power of crossing the legs, as is well shown in the illustration (fig. 6).

The Milk of the Patient with Adult Rickets

It was but natural that after investigating the calcium and phosphorus content of the blood of our osteomalacia patients, our attention should be drawn to the calcium content of the milk. As has been already pointed out, the babies of mothers with low calcium are very prone to develop tetany in the early neonatal period. Granted that they begin life with a deficient calcium content in their blood, how far is further trouble contributed to by a deficiency in the food? Some valuable information on this subject has been given by the work of one of our colleagues, Dr. S. H. Liu, and his co-workers [6] in the Nutrition Ward of the Department of Medicine. In that paper they present a very detailed study of three cases of osteomalacia, and two cases who showed no evidence of bony decalcification. We quote from their summary: "Four

of the subjects on low calcium intake had relatively small milk yield. The negative balance in calcium was not excessive, and calcium loss through lactation accounted for a small fraction of the total output.

" Moderate addition of calcium failed to rectify materially the calcium loss, but vitamin-D administration was efficacious in reducing the stool elimination of the calcium so that a markedly positive balance was obtained.

" In one subject whose milk yield was high, the calcium intake had to be considerably increased to maintain balance even in presence of vitamin D.

" The two subjects without clinical skeletal decalcification behaved similarly to, and showed as marked response to vitamin-D therapy as those with osteomalacia, suggesting the existence of subclinical states of vitamin-D deficiency and calcium shortage in the bones."

It is a fact well known to us that the milk supply from these osteomalacic mothers tends to be very poor ; in fact, in some instances, Kuo found it difficult to get an adequate amount for analysis. This may be partially due to the fact that their calcium intake is so low. In previous papers we have shown that the calcium intake in the food is far below what it ought to be. This is also borne out by the work of Wu and Yen [7] who estimated that the diet of the ordinary North Chinese women did not contain more than 0·3 grm. of calcium daily. Liu *et al.* [6] suggest that " with low calcium intake, a safety mechanism comes into play by which milk production is reduced, so that the extent of calcium loss becomes much less than it would be otherwise, and that vitamin-D deficiency is a more important factor than low calcium intake in accounting for the mineral stress in lactation ".

The moral of this is that osteomalacia patients should have a much larger calcium and vitamin-D intake than is needed for the normal woman, in order to promote a reasonable milk yield for the child.

But is there an actual deficiency of calcium in the scanty milk supplied by these mothers ? It has been almost impossible to get twenty-four-hour specimens of milk, and the question arose whether random samples would give us a fair estimate of the calcium and phosphorus being supplied.

On examination we found that samples from the same mother, taken at different times during the day, gave results which were so near each other, that the figures given are a true index of what the bulk of the milk would contain. The following table gives the figures (average) which we have obtained. The normal figures were taken from many determinations in our wards, the quiescent osteomalacia cases were those who had been and mostly were under treatment with calcium and vitamin D ; and the active osteomalacia cases had been without treatment.

Comparison of Various Values.

Milk	Stage	Ca. (mgm. per 100 c.c. milk)	P. (mgm. per 100 c.c. milk)
Colostrum	(1) Normal	26·58	17·90
	(2) Quiescent osteomalacia	22·84	9·15
	(3) Active osteomalacia	17·35	12·02
Transitional	(1) Normal	24·31	17·63
	(2) Quiescent osteomalacia	24·97	15·13
	(3) Active osteomalacia	17·72	18·52
Late milk	(1) Normal	21·19	11·66
	(2) Quiescent osteomalacia	24·49	13·96
	(3) Active osteomalacia	17·41	13·56

It will be noted that the amount of calcium in the milk, even though concentrated and scanty, is much less in the active osteomalacia cases.

It is remarkable how rapidly a proper supply of calcium and vitamin D will affect the calcium content of the milk. We pointed out in our last paper how quickly proper treatment with calcium and vitamin D would bring the blood figures for calcium and

phosphorus up towards the normal; and it is clear that the same holds good for the secretion of calcium in the milk, as is shown in the following case whose history has been already given in detail :—

Mrs. T. L. F.

ACTIVE OSTEOMALACIA WITH TETANY.

Treatment—Tricalcium Phosphate and Calciferol.

Material	Milk		Blood	
	Ca	P	Ca	P
Post-partum	(mgm. per 100 c.c. milk)		(mgm. per 100 c.c. serum)	
4th day	12·31	12·82	4·0	2·6
8th day	18·24	12·50	8·4	5·0
15th day	21·73	12·20	9·9	5·48
20th day	19·32	15·62		

In view of the fact that in India the relation between anæmia and osteomalacia is very close we felt it would be interesting to go more deeply into the question of anæmia in our patients, and its effect on the supply of iron to the child. One of us (Lin) has been especially working on this matter, and although more remains to be done, Dr. Lin has enough data to show that in cases of active osteomalacia the child is born seriously handicapped as to its supply of iron.

Taking first of all a number of normal deliveries in apparently normal Chinese women in our wards, the average worked out as follows :—

Cord blood of healthy Chinese babies (born of unselected mothers not apparently suffering from disease) : Average red cells 5,332,800 ; average hæmoglobin 15·34 grm. From babies born of osteomalacia mothers under treatment or old healed cases : Average red cells 4,808,500 ; average hæmoglobin 14·4 grm. From babies born of mothers with active osteomalacia : Average red cells 3,770,000 ; average hæmoglobin 11·5 grm. With regard to the last figures it must be remembered that these active osteomalacia cases come into our hands, as a rule, somewhat dehydrated and exhausted, which may possibly give a higher figure in the cord blood than is really the case.

As to the normal figure for hæmoglobin in the cord blood of newborn babies, it is generally stated as being about 21 grm.%.

Nils Faxén [8] puts the figure still higher and gives the following : Average hæmoglobin level 23·2 $\pm$ 0·25 ; red blood corpuscles 5,780,000 $\pm$ 0·130.

OSTEOMALACIA AND ECLAMPSIA

Does the presence of osteomalacia predispose to eclampsia ? On previous occasions questions have been raised as to the occurrence of eclampsia in cases of osteomalacia.

As far as is possible in North China we have made special inquiry into this. One may ask the question in two ways :—

(*a*) Do osteomalacia cases exhibit eclampsia in any unusual proportion ?

(*b*) Have any of the eclampsia cases of which one has been able to get records exhibited osteomalacia ?

In reply to both questions the answer is in the negative, with the exception of one doubtful case.

Dr. Clow (personal communication) informs us that in the Taiyuanfu Hospital, Shansi, there have been 522 recorded cases of Cæsarean section for osteomalacia, and in none of these has there been any mention of eclampsia.

From October 1929 to November 1936 in this same hospital there were records of 312 osteomalacia cases, with 213 Cæsarean sections, and no record of eclampsia in any of them.

Out of 1,800 confinements in this hospital during the same period, there were six cases of eclampsia, and in none of these was there any sign of osteomalacia.

At Pingtingchow, Shansi (personal communication from Dr. Parker), there are accurate records for 1931–6. During these five years there were 120 cases of osteomalacia, and six cases of eclampsia, but in no case have the two been combined in the same patient.

At Showyang, Shansi, in ten years there were 373 patients with osteomalacia, none of whom had eclampsia in addition.

In the Peiping Union Medical College Hospital between 1921 and 1937, there were 7,567 labour cases with 151 cases of eclampsia and 124 of osteomalacia. In only one of these have the two diseases been combined, and in this case the diagnosis was doubtful. It was an atypical post-partum eclampsia, occurring about twelve hours after Cæsarean section, the patient making a good recovery.

So that one can definitely say that osteomalacia does not predispose a patient to develop eclampsia.

At the time of our last paper we were already aware of certain degenerative processes which are occasionally seen in connexion with osteomalacia. One of us, Pi [9], took up the study of cataract in our osteomalacia cases, and in relation to what is known as "Cataracta tetanica." As cataract has hitherto never been especially associated with osteomalacia the subject is important, and also because the term "cataracta tetanica" is, in some cases at least, obviously a misnomer.

This cataract has to be looked for, as subjective ocular symptoms are slight; and as the majority of our osteomalacia patients are illiterate, it is only when the disease has considerably advanced, that they are likely to complain of loss of vision. What is the incidence of the trouble in osteomalacia cases? We have records of 124 osteomalacia cases admitted to the Peiping Union Medical College Hospital, and Pi, who examined about half of these, found 13 cases of this form of cataract amongst them. So it is probable that the incidence is about 20%. Under appropriate treatment these cataracts undoubtedly improve but do not disappear.

We have observed three other degenerative processes in cases of osteomalacia. These are not peculiar to osteomalacia, but are, rather, manifestations of avitaminosis in patients who are known to be deficient in vitamin D; and it is probable that where they occur in connexion with osteomalacia the underlying cause may be a mixed vitamin deficiency. They are: (*a*) Keratomalacia; (*b*) a peculiar form of failure of nutrition of the nails; (*c*) keratoses on the cheeks and over the elbows.

(*a*) *Keratomalacia.*—One of us [10] has previously reported a case of fœtal keratomalacia in an infant born from an osteomalacic mother. In this case it was impossible to get roentgenograms to determine whether the baby was also suffering from fœtal rickets. This case was kindly seen and verified by Dr. Pillat.

But the combination of rickets and keratomalacia is probably not so uncommon in this region as might be supposed. During five years there were as in-patients in the hospital in Peiping at least 10 cases of keratomalacia and proved rickets in infants under 2 years, and of these 10 cases, three were under 3 months of age and two under 4 months. Granted that these infants might not have shown roentgenological evidence of rickets at the moment of birth, it is not unlikely that if it had been possible to get sections of the epiphyses there might have been microscopical evidence of commencing rickets, and they are a striking commentary on the supposed absence of rickets in North China. And it is clear that where one gets deficiency of one vitamin, one is very likely to get a deficiency of more than one.

(*b*) *Nutritional disturbances of the finger nails.*—Two of our osteomalacia cases especially showed certain nutritional defects in the finger nails.

The first case came in on December 26, 1932, with very low blood calcium and marked osteomalacia. A Cæsarean section had to be done on January 13, 1933, tetany of the uterus having supervened. She made a good recovery. On April 21, 1933, her

finger nails were found to show certain nutritional defects. A second photograph was taken on June 9, 1933, showing marked improvement. There was no attack of abdominal pain in this patient.

The second case came in on March 4, 1933, with tetany and pregnancy.On April 13 she began to run a temperature and developed a subacute dysentery (Shiga). The first photograph was taken eight days later and shows the affection of the nails well established. By April 29 the dysentery was over. On May 21 a Cæsarean section was done, and she was discharged well with her baby on July 10. On July 21 the second photograph was taken, showing that the morbid process had been quickly arrested. Whether or not the dysentery played any part is doubtful.

The exact cause of these nutritional defects is not clear ; the rate of growth of the nail in this second case was about 0·15 cm. per month.

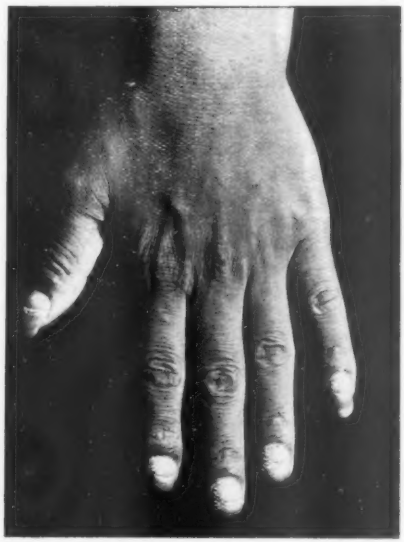


Fig. 7.—Nutritional disturbance of nails.

(*c*) *Nutritional disturbances of the skin.*—It has also been noticed that in some of these osteomalacia cases there is a marked dryness and scaliness of portions of the skin.

We have seen more than one example of this disturbance of nutrition, and think there is little doubt that it is due to an avitaminosis, though one hesitates to say which of the vitamins is involved.

It is clear that our original contention that osteomalacia was not a disease *sui generis*, but rickets in the adult, was correct. It is also clear that fœtal rickets, where adult rickets is present in the pregnant woman, is not uncommon, and that it presents clinical and radiological symptoms rendering it easy to diagnose; that where the affection has not progressed to the point of definite clinical symptoms, microscopical evidence may be present and that there is a definite tendency to the development of tetany and infantile rickets in the newborn child.

It is also clear that the cord blood in these cases of fœtal rickets presents definite deficiencies in calcium, phosphorus, and iron. Premonitory symptoms of adult

rickets such as thigh and back pain, excessive movements of the fœtus *in utero* and instability of gait should be kept in mind in antenatal examinations and the appropriate treatment given for the trouble.

Finally, it should be borne in mind that a mother with the signs of adult rickets is likely to be iron-deficient, and this deficiency, unless corrected, will be transmitted to the newborn child. The tendency of patients with adult rickets to suffer from opacities in the lens of the eye is an additional reason for careful and early treatment of the disease in general.

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Discussion.—Mr. V. B. Green-Armytage said he had first seen osteomalacia in Calcutta thirty years ago, and since then, although he had seen and collected a consecutive series of 500 osteomalacic patients in Calcutta, not once, despite their anæmia, their albuminuria, and their blood metal shortage, had the state of toxæmic eclampsia occurred. This was a point of some importance just at the moment when the Peoples National League of Health was spending quite a lot of time and money upon an experimental diet and vitamin supply to hospital antenatal cases. Would this experiment prove anything in view of the facts also recorded by Professor Maxwell? One point of great import did evolve from this paper, namely that in the depressed areas and where nutrition was at its lowest, one might expect to find in the rising generation a large increase of android or funnel pelves which might be missed by a too-casual or careless antenatal clinic. These cases were commoner all over the world to-day and there could be little doubt they were related to a vitamin calcium phosphorus deficiency in the food.

Prof. F. J. Browne said so far as he knew this was the first clinical demonstration that the experimental work of May Mellanby was applicable to human beings. We usually emphasized the importance of vitamin D and calcium in the diet of the expectant mother in order to prevent dental caries in the child, but there had lately been a tendency to stress the influence of heredity in the causation of dental caries and to minimize the importance of the mother's diet. Professor Maxwell's work seemed to prove that whether or not heredity played a part in dental caries the diet of the mother was also important.

Dr. Kathleen Vaughan said that in Kashmir the boat women and others who lived in the open air on the coarsest food never had the disease. Osteomalacia was considered to be hereditary by many Kashmiris themselves, but was really due to the social custom prevailing in high-class families of observing "purdah" or the seclusion of women. This usually entailed the women living in dark ground-floor rooms, the only light coming from small windows near the ceiling, placed there so that no man passing by could look in. Branches of the same family living in the country and going out freely were free from it, and sometimes a woman developed it only when her husband moved to a more densely populated part of the town and shut her up strictly in semi-darkness.

Although the softening of the bones was caused, just as rickets was caused, by absence of sunlight, yet the deformity produced was determined by the posture habitually assumed by the patient; thus sitting on the floor with arms clasping the legs produced a pelvis with an elongated conjugate, whereas sitting on chairs in European fashion tended to increase the transverse diameter. Later on, with further softening, the walls of the pelvis seemed to fall in, in all directions, and we had the Y-shaped pelvis typical of acute osteomalacia.

DISCUSSION ON CARCINOMA OF THE VULVA

Malignant Disease of the Vulva

By MORRIS M. DATNOW, F.R.C.S.E.

Introduction.—In recent years one has been called upon to treat malignant disease of the vulva more often than in the past, and this frequency has naturally stimulated interest and the obvious surmise that epithelioma vulvæ is more common in the Liverpool district than the literature would lead one to expect to be the case for the rest of the British Isles. In conversations with gynæcologists, the impression is usually obtained that the condition is rare.

I have seen and operated on 12 cases during the last two years, but this apparently large number for so rare a disease may have been referred to me because it was known that I was especially interested.

Incidence.—Brady [1] gives the total admissions to the Johns Hopkins Hospital since it opened as 165,000; 39,000 were gynæcological cases, and of these malignant disease of the vulva numbered 17, clitoris 6, labium majus 5, labium minus 1, fourchette 1, Bartholin's gland 1, too extensive to determine the situation 4. During the same period 756 cases of cancer of the cervix and of the urethra were operated on. Graves and Smith [2] found 21 cases of vulval cancer amongst all the material of the Free Hospital in Boston. Most of the growths were squamous-celled epithelioma.

Pathology.—Although all varieties of malignant disease are found on the vulva, my cases have been squamous-celled carcinoma.

Age of the patient.—Whilst cancer of the vulva is essentially a disease of old age, it has been described at all ages from 10 to 90. Lovegren [3] states that he has seen an inoperable squamous-celled cancer of the vulva involving the vagina in a child 17 months old. Wolf [4] gives the average age as 50·7 years. Dittrick [5] collected 135, the youngest was 20 years of age and the oldest was 90. The average age was unusually high, namely 70 years. 84% were over 45 years of age. Schreiner and Wehr [6] discuss 118 cases of which 9 (7·6%) were under 40, 30 (25·4%) between 40 and 50 years, and 79 (67%) over 50 years of age.

Ætiology and causation.—Graves and Smith believe that sexual abuse plays a part in the ætiology of kraurosis. Berkeley and Bonney [7] state that the incidence of carcinoma vulvæ would be reduced by half if all cases of leucoplakia could be effectively treated. Taussig [8] in 1931 re-states this. Graves and Smith found leucoplakia and hypertrophy in 16 of their 21 cases and kraurosis and atrophy in 14. In the five cases where neither atrophy nor hyperplasia was found, the growths were too far advanced or the specimen too meagre for a proper study. In our own material leucoplakia was always present. Seeking other causes, it is interesting to note that Brady reports a case of epithelioma which developed in a syphilitic lesion of the vulva. Ritchie [9] records a case of cancer of the fourchette in a patient aged 26 who had a construction operation when aged 13. Taft [10] describes a growth in a negress during the late stages of pregnancy at the early age of 16.

Site of the disease.—Carcinoma may arise in any part of the external genitalia, and in a paper with the late Blair-Bell [11] we mention a classification of the main sites of the disease as recorded by Taussig. Above, I have already given Brady's figures. Ederle [12] found in a collection of 677 cases of vulval cancer that the disease started in the clitoris in 109. In our series 18 (two of these involved the clitoris) occurred on the labium majus, 8 (1 involved clitoris) on the labium minus, 7 on the clitoris. The labia majora and the clitoris are the sites most often primarily affected, but in many cases the disease when first seen has spread so widely to adjacent parts as to make it difficult, if not impossible, for the observer to discover where it originated.

Diagnosis.—Is readily made in old people, but one has to be more careful with younger individuals. A differential diagnosis from tuberculosis and syphilis may be necessary in lesions with superficial ulceration. Tertiary syphilitic manifestations too, with nodular hyperplasia and ulceration may cause difficulty in diagnosis. Biopsy is a certain method of diagnosis.

In all patients there appears to be a rather long period of discomfort before they actually apply for treatment. There is a general consensus of opinion that leucoplakia vulvæ is a predisposing condition. The cancerous process seems to spread slowly at first, often giving rise to local implantation before involving the glands. The ulcerating type involves the lymphatics more readily. In the early stages pruritis or a burning sensation of the vulva is experienced by the patient. Later, she complains of a lump or of swelling of the parts. In the later ulcerating phases, a blood-stained offensive discharge occurs, and there may be considerable pain. Should the urethral orifice be involved, urinary discomfort and difficulty may supervene and later, incontinence. Constitutional symptoms are usually absent until the later stages, and distant metastases are rare.

Progress and prognosis.—As pointed out above, the growth is slow in its initial stages, but later it progresses more rapidly, and may soon cover a large area of the vulva. Contact lesions are sometimes seen. The first lymphatics to be involved are those in the inguinal and femoral regions, and ultimately the pelvic glands on the iliac vessels. Distant metastases are unusual, but have been found in almost all the organs of the body including the heart muscle ; and we have seen a case of general dissemination in the skin of the trunk and limbs. Ewing [13] states that in untreated cases death usually supervenes within two years of the discovery of the growth. The infection which is always present in ulcerated lesions, together with repeated hæmorrhages, undoubtedly contribute to the final issue. As the deeper structures become involved pain may be very severe and difficult to relieve. Clinicians refer to carcinoma of the vulva as a very intractable and fatal type of malignant disease. Treatment is frequently not sought by the patient until the condition is advanced. Rentschler [14] reported 71 cases treated in the Mayo Clinic by surgery, irradiation, and by a combination of the two methods. Of these, only 13 (18·3%) were alive and free from the disease at intervals between one and fifteen years. Tausch [15] recorded 39 cases of which only 7% were absolutely cured, although 15% lived for over five years. Schulz [16] has described 23 cases, and of these 13% were alive five years after the operation.

According to these figures it would appear that clinical cures of five years' duration must not be expected in more than 15% of cases submitted to operation, and that absolute cures are obtained only in about 7%. On the other hand Rupprecht [17], and Stoeckel [18], and others, take a more favourable view of the prognosis. Taussig [19] states that 60% of the vulval cancers seen by him were operable. Epithelioma which developed on a basis of leucoplakia were less malignant than those associated with syphilitic lesions. He found that after a complete vulvectomy with the removal of the lymph-nodes on both sides, the operated cases showed a five-year survival rate of 81·8%. This is higher than any other reports in the literature. Our results are given in the table on page 44.

Treatment.—Local excision or incomplete removal tends to disseminate the disease and hasten the end. Our experience with radiotherapy has not been fortunate, and we now always resort to radical excision. The literature indicates that surgery is steadily gaining favour and gives better results, although I am hoping that improved radium technique will finally lead to better results, as this is a form of treatment with a wider application and a far lower incidence of shock to the patient.

It has been pointed out by Kehrer [20] that the superficial lymphatic glands of the two sides are in anastomotic relation, and that the malignant lesion of one side of the vulva may infect the glands in the opposite inguinal region. This means that the

area over the mons veneris is the site of a network of lymphatic vessels, and accounts for the fact that local recurrence, when present, is frequently found in this region. The superficial lymphatic glands on either side are also affected with the deep inguinal, the obturator, and the pelvic glands on the same side. Some surgeons (Kehrer and also Stoeckel) suggest that operative procedures should be extended to include all those more distant lymphatic glands, but such an extensive operation on older patients could hardly be effected in one stage without a high mortality. Moreover, such measures are not really justifiable, for if the iliac glands are involved the disease has probably extended further. Clifford White [21] has abandoned block dissection and now carries out the operation in stages. By a radical operation, we generally imply that procedure which aims at the removal of the superficial inguinal and femoral glands on both sides in one piece with the vulva. The external genitals, together with the skin and underlying tissues over the mons veneris, are removed as widely as possible in accordance with the extent and position of the growth which may even involve the peritoneum and all the leucoplakic area if there be one. When the orifice is involved the distal portion of the urethra should be excised. The diathermy knife is helpful although not essential, and spinal anæsthesia diminishes the amount of bleeding and lessens the shock to the patient. The exaggerated Fowler position helps in the subsequent healing of the wound.

NUMBER OF CASES——35

Average age (32 *patients*) ..	63 years	*Treatment and results*—	
Oldest ..	78 years	Radical operation done	32—1 died of sepsis
Youngest	23 years		1 died of hæmorrhage
Nature of disease			5 died of disease
Squamous-cell carcinoma ..	34		1 died of intercurrent disease
Spindle-cell carcinoma ..	1		3 not traced
Primary lesion ..	22		
Recurrent lesion ..	3		
Site of lesion			
Labium majus .. .. (2 of these involved clitoris)	18	Radium followed by radical operation	2—1 died of disease
Labium minus .. .. (1 involved clitoris)	8	Radical operation followed by radium ..	1—died of disease
Clitoris	7	Known to be alive 5 and more years	10
Vestibule and urethra ..	2	Known to be alive 1-5 years ..	9
		Known to be dead	10
		Not traceable ..	3

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The Treatment of Carcinoma Vulvæ

By Percy Malpas, F.R.C.S., F.C.O.G.

In no variety of cancer does the choice of the proper treatment present such a difficult practical problem as is the case with carcinoma vulvæ. There are several reasons for this difficulty, reasons I suppose very similar to those formerly experienced in determining the proper treatment of carcinoma cervicis. One of these reasons is that carcinoma vulvæ is not quite common enough to enable any one man to acquire a wide experience. It seems indeed as important to have some central body collect and assess unified records of carcinoma vulvæ as is done in the case of carcinoma cervicis by the League of Nations Radiological Subcommittee.

The second reason is that carcinoma vulvæ is a protean lesion, varying from an actively growing tumour in comparatively young women to a slow superficial ulceration in an old patient who has in any case a low expectation of life.

Prior to 1925 radical vulvectomy was the only method available. From that date onward increasing attempts were made to deal with the cases by irradiation. The attempt to use radium undoubtedly sprang from a general experience that the results of radical vulvectomy were often unsatisfactory. Otherwise there would have been no sense in departing from a very attractive method of treatment. Radium therapy in turn then fell into disrepute because of the high incidence of radium burns and local recurrences, although the treatment was carried out on principles similar to those already giving good results with cancer in other sites. It is only in the last four or five years that these earlier mistakes have been corrected. Dr. Ellis, the Director of the Radium Centre in Sheffield, showed us at the North of England Obstetric and Gynæcological Society last year, some beautiful results of irradiation therapy, and as a result of his and other workers' reports the time has come when irradiation can be weighed seriously against radical vulvectomy.

My own experience is based on 39 cases, either my own or entrusted to me by my seniors, Doctors Willett, Leith Murray, Burns, and Professor Leyland Robinson. Nine of these cases were hopelessly advanced when first seen and no treatment was possible. The other 30 were treated in a variety of ways: radical vulvectomy, local excision of the growth, interstitial and surface irradiation of the primary growth with and without excision or irradiation of the regional glands. In 14 cases the glands were not enlarged. In the other 16 they were involved. Three of the cases were local recurrence after a vulvectomy had been performed, in one instance nine years previously. In this case the recurrence was treated with interstitial radium and she is still living another six years after, that is fifteen years after the first operation. In this connexion it is interesting to note how slow-growing many of these cancers can be. It is a disease in which a permanent cure rate can scarcely be given.

The selection of the mode of treatment for any given case must be eclectic; no one treatment so far is universally applicable and must take account of the following factors:—

(1) The state of the regional lymph-glands.
(2) The site, type, and extent of the growth.
(3) Its rate of growth.
(4) The condition of the rest of the vulva, i.e. healthiness of the skin, vascularity, extent of menopausal and senile atrophic changes.
(5) The general condition of the patient.

Certain general principles also govern the choice of treatment or rather the lines on which we should develop our treatment. In the first place, carcinoma of the vulva behaves and reacts in the same way as carcinoma of the skin in general, though its behaviour and reaction to treatment are somewhat modified by the special local

conditions which obtain. In the treatment of skin carcinoma the use of radium is gradually ousting radical surgery, and for this reason alone radium is likely to prove of more value in the future in the treatment of carcinoma vulvæ.

In the use of radium in the vulva, as in the skin, the same special precautions must be taken to eliminate necrosis, because skin is relatively intolerant of irradiation as compared with other tissues. The second important factor modifying radium treatment in this site is the special nature of the blood supply of the vulva. Donaldson, in his remarks on Spencer's case of vulval carcinoma, stressed the point which is becoming recognized more and more, that the effect of radium depends as much on its action on the tumour bed as on the tumour. Nearly all the vessels supplying the vulva come from the pudic artery, and these vessels are practically end-arteries. If they become occluded by over-irradiation there is little or no collateral circulation, and healing will be slow and secondary necrosis likely. Todds' hypothesis of a massive occlusion of the posterior segment of the pelvis as a cause of rectal ulceration following irradiation of a carcinoma cervicis is even more applicable to the vulva.

The third special factor to be considered is that after the menopause the vulva undergoes a progressive atrophy and the more atrophy develops the more difficult it is to obtain a healthy reaction to radium.

Finally, while the free lymphatic communication between all parts of the vulva has been borne in mind by those who have devised the radical operation, it has often been forgotten in radium therapy. If radium is to be used the whole vulva, including the mons and the perineum, must be irradiated. Just as we properly speak of a radical vulvectomy, so we should speak of a radical irradiation. It is not enough to irradiate the tumour and its surroundings alone ; and for this reason it does not seem quite sufficient to base the dose of radium to be used entirely on the volume of the tumour as in some systems of radium dosage. The dosage must be based on the area of the whole primary lymphatic area.

In cases where the primary growth is mobile and the glands are not involved, radical vulvectomy is probably at the moment the method of election, but if the lesion is very slow-growing—and it is not uncommon for these lesions to remain localized for months if not years—radium is to be preferred because it does not break down the local resistance to the spread of the growth which is present in such cases. Vulvectomy is certainly preferable in cases of diffuse leucoplakia with small growths. Thereby precancerous tissues are removed and the patient's complaints of pain and pruritus are relieved immediately.

Whether the glands should be removed is always a moot point. If they are not enlarged and the lesion is active then there is no doubt gland dissection should be done. In old and feeble women, when the cancer is growing slowly and surgery is decided upon, there is much to be said for contenting oneself with free vulval excision alone. The glands in such a case should be given deep X-ray therapy provided an efficient apparatus is available.

Necrosis and sloughing of the flaps of the inguinal wounds is notoriously troublesome. This can be obviated by leaving the inguinal wounds or the inguinal segments of the complete operation quite open without any sutures. No dressings at all are applied to the wounds except some gauze below to catch any discharges. A cradle is placed over the patient and a 60-watt lamp fixed to it. This lamp is only switched off when the patient feels uncomfortably warm. It is important to resist the temptation to put in even one approximating stitch. Although the wound may be a hand's breadth at the end of the operation, after a week it will commence to close rapidly, and in three weeks will be completely closed with a fine linear and almost invisible scar. If the wound is sutured it serves as a collecting place for all the lymph from the legs, vulva, perineum, and anal canal. Infection from within is unavoidable.

Radium therapy is the method of choice even in early cases without glands, under the following conditions :—

(1) When the vestibule is involved.
(2) When the lesion is large, or multiple ulcers are present.
(3) Poor general condition.
(4) Slow-growing lesions.
(5) An amenable patient.
(6) Local recurrences after vulvectomy.

With the exception of urethral carcinoma, which is really a separate problem and requires a cavity technique, most vulval cancers are best treated by an interstitial technique. Provided certain conditions are satisfied, there should be little or no fear of subsequent necrosis or local recurrence.

I have already referred to the need for radical irradiation of the whole primary lymphatic area up to the site of the first gland station, i.e. the irradiated areas must extend outwards as far as the inner ends of the inguinal canals and upwards well on to the mons veneris. Estimation of the amount of radium necessary based on the volume of the tumour is not enough ; it must be based on the surface area of the vulva as well.

The duration of exposure is of the utmost importance, more so in the case of the vulva than elsewhere. Ninety-six hours has been the utmost limit of tolerance in our experience in Liverpool. We have been using needles of approximately 1 mgm. per cm. active length and with needles of this intensity this time must certainly not be exceeded. Overdosage is disastrous, and uniform insertion of the needles is essential. They are introduced at 1 cm. distance over the whole vulva including the growth. Where necessary one, two, or even three planes 1 cm. apart are used. The needle should be introduced to lie parallel to the skin at a depth of 0·5 cm. Dr. Ellis of Sheffield has stressed a most important point in the technique. The patient must be nursed lying in the position which she occupied on the operating table. If she changes her position on return to bed the needles no longer maintain their intended spatial relationships.

In most cases the needles are best inserted with the patient in the dorsal position with the knees drawn up and kept well separated. I have found the left lateral position is not tolerated very well by older women.

The needles are kept in position by Columbia wax or rubber packs which are best covered with lead foil to protect the surrounding parts. These packs serve to keep the labia apart. An indwelling catheter is desirable in many cases, and this can be brought through a hole in the pack and secured to it.

In the after-treatment it is desirable to avoid hot baths, friction with the clothes, irritating applications. A cod-liver oil ointment is as good a dressing as anything.

Unfortunately more than half the cases present glandular involvement when first seen, and although some treatment is essential for these, the end-results are disheartening and tend to obscure the good results certainly obtained in the earlier cases. Many are quite hopeless, and all that can be done is to minimize the discharge. Diffuse diathermy coagulation, as used to be practised for carcinoma of the tongue, is sometimes of service, but radium to the primary lesion gives surer results. Even a hopeless growth will often clean up in a few days with the interstitial technique. Excision gives unfavourable results in advanced cases. The wounds heal poorly and often the only result is an increase in the patient's sufferings.

Gland dissection is contra-indicated once the glands are clinically enlarged. They may be tackled with interstitial radium or deep X-ray therapy. Many of the glandular enlargements are inflammatory, and if the primary growth is amenable to treatment it should certainly be dealt with. The state of the glands and their treatment is really the key to the whole problem ; if they are involved surgery is of no avail, if they are not involved the critical might ask why deal with them at all. I have seen

one or two cases where rapid dissemination of the growth followed excision of enlarged glands. Interstitial irradiation of the glands has been widely practised, but the lymphatic areas are so extensive and so irregular in shape that uniform irradiation by an interstitial technique must be almost impossible, and the hope of further advances lies probably with some form of teleradiation.

With regard to the management and treatment of recurrences it is difficult sometimes to distinguish between a glandular recurrence and a radium ulcer; indeed the appearances of both are identical. I have found the best diagnostic criterion is the site of the ulcer. If it occurs away from an efficiently irradiated area then it is a recurrence or persistent growth. Local recurrences after radiation, as well as persistent radium burns, call for excision, though there has been a tendency to excise vulvas after interstitial radium before giving the burns a chance to heal. Recurrences can be treated by interstitial radium. Superficial recurrences may sometimes be treated by a Chaoul contact tube. We have had one successful case treated with this; another in which the ulcer was deep failed completely. It is, at all events, worth while to deal with recurrences, as often survival for another year or two will be obtained thereby.

Epithelioma of the Vulva

By J. Eric Stacey, M.D., F.R.C.S.

In Sheffield in ten years we have had roughly 150 cases of epithelioma of the vulva. This is a very much greater incidence than for the country as a whole, and is a position shared by the cotton-spinning districts of Lancashire and dye-works district of Halifax. In fact, Dr. Henry of the Home Office, in an analysis of cases to compare with the incidence of epithelioma of the scrotum, found that between 60% and 70% of the cases were engaged in processes involving the use of bituminous oil. I have not had adequate time to prove the same incidence in Sheffield, but quite a number of my patients had been buffer girls working in the silver and cutlery industry for very many years, both of their youth and married life. In a few of these I have been able to elicit the information that they were in the habit of using oily cotton waste in their lavatory toilet.

On reviewing the treatment of this disease as carried out at the Jessop Hospital for the past ten years, I find there has been a gradual evolution from the days of treatment by surgery alone, through a phase of treatment by radium alone (in the cases of some of my colleagues), to a middle course of a judicious use of radium combined with diathermic surgery. With more perfected radium and X-ray technique I can visualize the abandonment of surgical methods except in a few selected cases—an advance which is generally accepted now as the line of treatment for carcinoma of the cervix.

Up to 1932, when Frank Ellis commenced duty as Director of the Sheffield Radium Centre, our efforts at radium treatment of cancer of the vulva were sporadic and sketchy, for the reason that we lacked the radium and did not possess the skill in its use even had we had it!

I wonder if I am putting my head in the lion's mouth when I say that the lack of skill in the use of radium for cancer of the vulva was strikingly prevalent everywhere else before this date and still is so except in the hands of a few experts.

Before 1932 I can find the records of only five cases treated by radium in Sheffield, and in two of these vulvectomy had first been unsuccessful. In two others vulvectomy was performed because the radium was unsuccessful and the fifth case was as hopeless from the start as the other four were a few weeks after their treatment.

From this date, 1932 onwards, radium was used increasingly in the treatment of cancer of the vulva up to 1935, but the cases handed over to Ellis for radium treatment

were often those which were looked on as, for some reason or other, inoperable, or where recurrence had occurred after operation.

At this period, 1932–5, the radium results were often disappointing, and I published in 1934, in the *Transactions* of the North of England Obstetrical and Gynæcological Society, five cases of vulvectomy being necessary after treatment of seven cases by radium. In every case there was a radio-necrotic ulcer in some patch of which epithelioma had either recurred or had not been cured by the radium in the first place.

From 1935 onwards a far better technique has been carried out in the treatment of these cases; of my own seven cases treated primarily with radium I have had to perform vulvectomy on only two—one for necrosis and one for epithelioma. Of all the 36 cases treated by radium primarily in 1935, 1936, and 1937, vulvectomy has only been subsequently necessary five times. Where radium is used as a primary treatment, it is inserted with the application of the following general principles :—

(1) Radium needles are inserted in such a position of the patient that they maintain the desired spatial relationships to each other and to the growth. Therefore the patient is nursed in the same position as that in which she was for the insertion of the needles.

(2) Material (sorbo rubber) is used to hold radium rather than implanting tissue unnecessarily to get homogeneity, and to keep parts such as the buttocks at a known distance from each other.

Application to Special Cases

(1) Anterior end of vulva affected—needles are inserted with patient in supine position.

(2) Posterior end affected—patient in left lateral position.

(3) Whole vulva affected—patient in lithotomy position. These positions are maintained until the radium is removed.

This is the method employed in the local treatment. Where there are obvious glands, or where it is deemed necessary to treat the glands, the method employed is :—

Glands

Patient in supine position.

Groins cleaned with spirit.

Two planes of radium are used where any glands are greater than 1 cm. diameter.

Small plane at a measured distance from larger deep plane, superficial to enlarged glands.

Needles fixed with stitches or elastoplast. Dry dressing.

Details of Radium Application

Distance apart of planes—2 cm. best distance unless planes 12 cm.^{2} only then 1·5 cm.

Distance apart of needles :—

If uniform intensity	1·5 cm.
If peripheral needles $\frac{3}{2}$ × intensity of others	1 cm.

After-treatment is important, and is as follows :—

Necrosis	No hot baths
Dermatitis	No ointments
Moist desquamation—	
Groins	Dry dressing
Vulva	$\frac{1}{2}$% arg. nit. on gauze
Slight necrosis	$\frac{1}{2}$% arg. nit. (moist dressing). Later lotio rubra
Marked necrosis	Diathermic excision
Residual malignancy	Excision

We grade our cases in Sheffield into five stages :—

(1) Operable primary growth.
(2) Operable primary growth with mobile accessible glands.
(3) Inoperable.
(4) Recurrence.
(5) So extensive as to be hopeless.

I am not proposing to discuss the relative merits of radium against surgery by a statistical review of the survival rate in the various methods of treatment, because to get a comparison with Taussig's five-year survival rate after Bassett's operation as published by him in 1929 would be comparing an established method of treatment with an experimental one. There must be few observers bold enough to maintain that the treatment by radium was more than in its infancy five years ago. For my own part I think it is still somewhat in the experimental stage.

My observations are based on a survey of all the cases treated by every method in the Jessop Hospital from the beginning of 1935, i.e. 38 cases, of which 15 were my own personal cases. Also all the cases treated in Sheffield by radium as the primary treatment since the beginning of 1935, when the new technique was elaborated by Frank Ellis, to the end of 1937, i.e. 36 cases.

I find on tracing my own personal cases for ten years I have had 36, in all of which 15 occurred in the period from 1935. This does not mean a greater incidence of the disease because nearly half of them occurred in three years, but that I personally during the years mentioned had twice the number of beds under my care that I had previously. The actual number of cases seeking treatment in the Sheffield area, with a fairly stable population, is roughly 17 a year.

Of the 36 cases treated by radium in the years 1935, 1936, and 1937 :—

Alive 1937	9 out of	14
1936	8 out of	13
1935	3 out of	9
	20	36

20 are alive to-day, i.e. 55%.

The method of treatment of the 38 cases occurring in the Jessop Hospital from 1935 onwards was as follows :—

	No. of cases
Radium to growth	12
Radium to growth and glands	10
Excision followed by radium	2
Radium followed by excision	3
Local excision and radium to glands ..	2
Local excision alone	5
No treatment	4
	38

In ten years, the treatment given to my own personal 36 cases has been as follows :—

	No. of cases
Extensive vulvectomy with excision of glands	8
Local vulvectomy	12
Primary radium to vulva (2 of these subsequently had vulvectomy—1 for necrosis and 1 for recurrence)	4
Primary radium to vulva and glands (5 of these subsequently had vulvectomy for necrosis and recurrence)	10
No treatment other than nursing	2
	36

From a comparison of this with the 38 cases distributed among all the Jessop Hospital surgeons, it will be seen that I favour radium less than some of my colleagues.

Of the 36 cases in which radium was used in 1935, 1936, and 1937, five cases have had excision performed after the radium treatment. Two of these were for radium necrosis and three for the recurrence of the epithelioma. Thirteen had further treatment for some kind for recurrence, out of 36 radium cases.

The average age of my cases is 63 years, the youngest being 47 and the oldest 80.

Certain factors are offered for discussion as contributing to failure with radium.

Extensive growth.
Poor blood supply and lymph drainage.
Previous operation or other scarring.
Overdose.
Underdose.

To sum up the pros and cons of radium against surgery :—

For radium	*For surgery*
No shock.	No necrosis.
No operative mortality.	Less subsequent discomfort.
No mutilation.	Removes " precancerous " tissue.
Minimum danger to urethra.	Can deal with iliac glands.
Wider application, e.g. fixed glands, inoperable growths.	

Against both
Danger of recurrence.

For both
Can cure cancer.

Discussion.—Dr. FRANK ELLIS : Firstly I agree that radium treatment of carcinoma of the vulva is still in the experimental stage. The cases which I showed to the North of England Gynæcological Society were shown purely with a view to demonstrate the possibility of obtaining a normal-looking vulva after radium treatment. All the cases have not been uniformly successful and the late results are not yet available. But, secondly, I should like to make the statement that, without careful and accurate work carried out on sound principles, the immediate results of radium therapy, especially in cases of vulval carcinoma, will be very disappointing, besides resulting in conclusions regarding the possibilities of radium therapy which are unjustifiably harsh.

Data concerning the rational use of tissue-dosage in radium therapy have been published in the *British Journal of Radiology* by Paterson and Parker, and others have appeared subsequently. There are rules given for the clinical use of radium which should be understood and followed by all who practise radium therapy. The important point is that the tissues treated should absorb radiation uniformly. To distribute the sources of radiation uniformly instead is quite wrong. I will not give details, as anyone who is interested can look them up for himself. I will stress the point, however, that any application of radium, unless carried out with scrupulous exactitude, is bound to fail, whatever rules are followed.

Thirdly I wish to emphasize the necessity, in dealing with radium, for ensuring that the radium maintains the position in which it was applied and for which the tissue-dosage is calculated. The application of this to carcinoma of the vulva is that the patient must be nursed in the position in which the radium is inserted, whether in the supine, the left lateral, or the lithotomy position.

Dr. HURDON : Cancer of the vulva is comparatively rare and there are no large series of cases on which to base a definite opinion regarding the most effective method of treatment. The exceptionally good results obtained by Mr. Malpas prove the value of the radical surgical treatment of suitable cases. It has always been the view of my colleagues and myself that favourable cases should be operated on ; the cases treated by radium therapy at the Marie Curie Hospital have been technically inoperable or operation has been contra-indicated on general grounds, and especially because of advanced age. Though vulval cancer sometimes occurs in younger women it is essentially a disease of old age ; there is a relative incidence increase up to 75 years and over.

At the Marie Curie Hospital 114 cases have been treated by radium—72 primary, 41 recurrent after radical excision, and one case secondary to a cancer of the ovary removed a year before

Fifty-five cases—34 primary, 21 recurrent—have been treated more than five years with the following results :—

Primary cases,	34, living 8	—23·5%.
Recurrent cases,	21, living 10	—47·6%.
Combined cases,	55, living 18	—32·7%.

I have reported these cases to show that although operation is elected for suitable cases, some advanced cases, especially recurrent cancers, respond well to radium therapy.

Prof. F. J. Browne said that after listening to the discussion he thought a strong case might be made out for the centralization of the treatment of all cases of cancer of the vulva. In most hospitals only three or four cases a year were seen, some treated by radical operation and some by radium, so that it was impossible for any one clinician to gain sufficient experience to enable him to do the best for his patient. The radium treatment of these cases was a highly specialized business and progress in treatment was most likely to be made by those who had undergone special training and who were also given opportunity to treat large numbers of cases.

Section of Anæsthetics

President—R. J. Clausen, M.C., M.B.

[*December* 2, 1938]

Some Recent Work on Barbiturates

By Professor G. R. Cameron, D.Sc.Melb.

Abstract.—Toxic effects are sometimes seen after the administration of quite small amounts of barbiturates. Factors concerned in their production are discussed under the following heads :—

(1) Barbiturates can produce liver damage, even hepatitis.

(2) Barbiturates may become toxic in the presence of liver damage, as shown by :—

(*a*) Clinical and post-mortem experience.

(*b*) Experimental evidence—the work of Pratt and Koppanyi in America and our own experiments showing that certain barbiturates may exert toxic effects not only when there is severe liver damage but also in the early stages of liver injury.

(3) Other factors also seem to be concerned :—

(*a*) Cold.

(*b*) Hæmorrhage.

(*c*) Fasting.

(*d*) Sepsis.

(*e*) Tight bandage around upper abdomen.

(*f*) Castration.

The experimental evidence for this statement is given.

It is a matter of well-nigh universal experience now that from time to time toxic effects are seen after the administration of quite small amounts of barbiturates. The quick-acting members of the group, "nembutal" and evipan sodium, are more frequently concerned than the slow-acting forms such as barbital sodium and phenobarbital sodium. I wish to consider briefly some of the factors which I believe are concerned in these untoward effects.

(1) Although there is little reason to expect direct injurious effects in man with the doses employed, I know of several instances where the liver has been permanently injured after prolonged administration of "nembutal." One such case I am aware of through the kindness of Prof. James Miller, Ontario, Canada. Here "nembutal" had been administered regularly in large doses for a long time. Post-mortem examination disclosed a moderate degree of chronic hepatitis of a type one associates with continued poisoning. This result is, however, unusual.

(2) (*a*) *Clinical and post-mortem experience.*—There is a feeling amongst clinicians and pathologists that it is not wise to administer barbiturates even in small doses to subjects with liver disease. Some of the fatal cases have shown at autopsy severe liver damage, either acute, e.g. necrosis, or chronic, such as cirrhosis or advanced carcinoma. I have seen two such cases in the course of the last year, both with severe cirrhosis of the liver.

(*b*) *Experimental evidence.*—There is now much experimental evidence to show the influence of liver damage in enhancing the action of barbiturates. Pratt and his co-workers (1932, 1933) found that dogs given "nembutal" twenty-four hours after prolonged chloroform anæsthesia, sleep for a much longer time than normal animals.

Barbital shows no such effect when the liver is injured. It is known that barbital is almost wholly excreted by the kidneys, the liver playing little or no part in its removal; "nembutal", on the other hand, is believed to be detoxicated in the liver. Koppanyi *et al.* (1936) confirmed this work in cats and dogs, but obtained prolonged sleep also with barbital. They suggested that chloroform injures the central nervous system, so that nerve-cells become more susceptible to barbiturates. During the last fifteen months Dr. G. S. W. de Saram and I have been working on the relationship of liver damage and barbiturate action. We have studied the action of some members of the group on rats whose livers were severely damaged with carbon tetrachloride. Since we gave this poison subcutaneously, so that it was very slowly absorbed in small amounts, we felt that any action on the central nervous system was eliminated or reduced to a minimum: certainly the animals showed no evidence of central nervous system disturbance. Twenty-four hours after administration of CCl_4, at a time when the liver is severely damaged, there is considerable prolongation in action of "nembutal" and evipan. Three to four days after the administration of CCl_4, when repair is going on actively in the liver, the mean duration of sleep for a group of such rats falls within normal limits. The slow-acting barbiturates, "medinal" and "luminal", showed no significant prolongation of action after acute liver damage. We feel convinced, therefore, that severe liver damage modifies the action of the quick-acting barbiturates, probably through inhibition of some kind of detoxifying mechanism. We then studied progressive liver damage produced by giving rats twice weekly small doses of CCl_4 subcutaneously. A number of workers (*see* Cameron and Karunaratne, 1936, for literature) had found that a toxic cirrhosis of the liver could be produced in this way in three to six months. Table I (from the paper of Cameron and de Saram, 1939) summarizes our results.

TABLE I.—INFLUENCE OF PROGRESSIVE LIVER DAMAGE ON THE ACTION OF "NEMBUTAL"

Duration of liver damage	Number of rats	Mean duration of sleep in minutes after standard dose of "nembutal"	Standard deviation	Mortality following standard dose of "nembutal"
Normal	55	102 ± 4	42	0
One month CCl_4 intoxication	24	148 ± 14	55	12·5%
Two months CCl_4 intoxication	18	208 ± 10	65	28%
Three months CCl_4 intoxication	12	249 ± 22	106	58%

Standard dose of "nembutal" 40 mgm. per kg. body-weight, subcutaneously. The differences of the means are statistically significant. (From the *Journal of Pathology and Bacteriology*, 1939, **48**, 49.)

It will be seen that three months of CCl_4 intoxication, by which time the liver alone is grossly damaged, is sufficient to convert a mild dose of "nembutal" into one followed by serious results, viz. considerable prolongation in action and a mortality of 58%. But the interesting thing is that even after a short period of intoxication (one month) there is a significant increase in activity of "nembutal", and lethal effects are obtained in some animals with a dose well below the minimal lethal dose. At this stage the liver shows very slight alteration both to the naked eye and microscopically. A liver which presents little evidence of structural damage may in reality be incompetent functionally. It becomes more and more important that sensitive methods for assessing liver function disturbance should be sought for. Likewise it is obvious that a great deal more requires to be known about the factors which influence liver function, apart from structural damage.

(3) With this idea in mind we have been studying the effect of a number of simple procedures on the action of some barbiturates. These procedures have been selected because of their importance for patients to whom barbiturates might be administered.

Thus we have varied the body temperatures by exposing animals to draughts or by applying ice-packs to the upper abdomen. We have bled rabbits, simulating a severe hæmorrhage; others we have fasted; whilst to the abdomens of some we have attached tight bandages. We have also made some observations on the influence of sepsis and of castration. In all instances careful study of the liver and other organs at the conclusion of the experiments has failed to disclose any evidence of structural damage.

(*a*) The effect of applying an ice-pack to the liver region is shown in Table II. The rabbits were given "nembutal" intravenously in doses which produced sleep in

TABLE II.—ICE-BAG ON UPPER ABDOMEN DURING "NEMBUTAL" ANÆSTHESIA

Rabbit	Body-weight in grams	Duration of sleep in minutes	Result
1	1995	99	Recovery
2	2050	135	,,
3	2000	135	,,
4	2100	135	,,
5	2570	165	,,
6	1950	185	,,
7	2500	190	,,
8	1720	195	,,
9	1890	200	,,
10	2150	250	,,
11	2600	60	Died
12	2250	70	,,

20 control rabbits, under similar conditions, after the same dose of "nembutal", gave a mean duration of sleep of 109 minutes with a range of 60–160 minutes. All recovered. Standard dose of "nembutal" 33 mgm. per kg. body-weight intravenously.

normal animals for an average of 109 minutes, the range being 60–160 minutes. As soon as they were asleep, blocks of ice were applied to the upper abdomen, being attached loosely by adhesive plaster. Of 12 animals so treated, two died after 60 and 70 minutes respectively, others showed prolongation of sleep. Although the number of animals is small we believe these results suggest that cold may influence the action of "nembutal" in some cases. Similarly in a group of 13 rats kept in a cold draught during November whilst under the influence of "nembutal", 3 died. Their litter mates kept warm, recovered from the same dose of "nembutal" in the usual time.

(*b*) The effect of blood loss on the action of "nembutal" is illustrated in Table III. The amounts of blood removed varied from 22–30% total blood volume, corresponding

TABLE III.—THE EFFECT OF BLOOD LOSS ON THE ACTION OF "NEMBUTAL"

Rabbit	Body-weight in grams	% blood vol. lost	Interval between bleeding and administration of "nembutal" in hours	Duration of sleep in minutes
1	2600	9·7	0	135
2	2650	9·8	0	145
3	2110	11·3	0	135
4	2600	8·9	24	100
5	2100	10·6	24	110
6	2250	11·0	24	125
7	2550	22	23	85
8	2050	26	19	150
9	2400	25	24	150
10	1920	30	24	150
11	2300	28	24	160
12	2100	28	19	*210*
13	1950	23	24	*240*
14	2025	28	19	Died in a few minutes

Controls as in Table II. Standard dose of "nembutal" 33 mgm. per kg. body-weight, intravenously.

to a very severe hæmorrhage in man. About twenty-four hours after bleeding the animals were given " nembutal " intravenously. One animal died at once, two showed considerable prolongation of sleep, whilst the average duration of sleep for the survivors was 163 minutes as against 109 minutes for normals, a significant difference. This effect cannot be attributed to a decrease in circulating fluid for by the end of twenty-four hours the total blood volume has been restored to normal. The most likely explanation is that the sudden anæmia has either altered the sensitivity of the central nervous system or has inhibited the detoxifying mechanism.

(*c*) After fasting forty-eight hours, with no restriction of water-intake, two of a group of 10 rats slept for 330 minutes following a small dose of " nembutal " ; the mean duration of sleep in a large series of normal rats was 102 minutes with a range of 25–210 minutes. It seems likely that fasting may occasionally influence the action of " nembutal ". Whether this is concerned with depletion of glycogen store in the liver, a factor known to increase the toxicity of chloroform (Davis and Whipple, 1919) can only be surmised.

(*d*) There seems little doubt that sepsis may influence unfavourably the action of some barbiturates. Recently we conducted an autopsy on a woman with an ovarian abscess who developed acute yellow atrophy shortly after operation. Evipan had been administered ; the anæsthetic was gas and oxygen with a little ether. It was difficult to escape from the conclusion that sepsis, together with the barbiturate, was responsible for the liver failure. This view has been supported by our experimental experience, for occasionally we have seen greatly exaggerated effects following the administration of " nembutal " and evipan to animals with abscesses.

(*e*) The application of a tight abdominal bandage to rats and rabbits did not influence the action of " nembutal " so long as the animal was perfectly healthy. In one rabbit such a procedure resulted in death, but post-mortem examination disclosed a mild cirrhosis of the liver.

(*f*) Finally we have obtained an unexpected result after castration. A group of 18 twelve-month-old female rats, castrated at one month by our colleague, Mrs. Boycott, showed a mean duration of sleep of 223 minutes following the subcutaneous administration of " nembutal ", with a mortality of 22% (Table IV). Normal female

TABLE IV.—" NEMBUTAL " AND CASTRATION

Number of rats	Body-weight in grams	Mean duration of sleep in minutes	Mortality (%)
Castrated females—			
18	240–355	223 ± 12	22
Normal females—			
30	160–350	100 ± 4	0

The difference of the means is statistically significant. Standard dose of " nembutal " 40 mgm. per kg. body-weight subcutaneously.

rats of about the same body-weight recovered, on an average, in 100 minutes from a similar dose. The livers of such castrated animals appear healthy although the storage of fat in the liver cells seems to be increased. The explanation of this castration effect is obscure. After castration there is diminished metabolism (Loewy and Richter, 1899, Loewy, 1902), so that there might well be decrease in activity of the detoxifying mechanism for barbiturates and therefore increased susceptibility. Recently Hall and Korenchevsky (1938) have shown that the liver weight in male rats castrated before sexual maturity is less than that of normal rats, with a decrease in size of liver lobules. They suggest there is a physiological rather than a pathological decrease in function of the liver after castration. Further work is being continued on this subject.

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Discussion.—DR. EVA BYRDE : *Summary of results obtained by giving large doses of "nembutal" to women in normal labour.*—All cases were emotionally unstable women who had not responded to usual sedatives. The patients were divided into two classes : Those who were three or more days in labour, who were given a large dose of nembutal at least twelve hours before delivery ; and those whose labour was of normal length who were given nembutal within six hours of delivery.

(1) In long labours the following technique was adopted : Patient emptied her bladder, drank a lot of glucose lemonade and was given nembutal gr. vi by mouth, and then encouraged to sleep. Two hours later another drink of glucose lemonade was given, and drachms ii of syrup. chloral hydrate. Bladder was emptied again, and patient left as quiet as possible. Four hours later nembutal gr. iii was given, and two hours after this a further drachms ii of syrup. chloral hydrate. If delivery had not occurred within four hours of this dose, a further gr. iii of nembutal was given. Only two cases fell into this category ; these were given nembutal gr. xii in eighteen hours ; all others had gr. ix in fourteen hours.

Effects of nembutal were first a period of complete sedation for about six hours, from which the patient could be roused enough to be fed, followed by a period of delusion, restlessness, and lack of co-operation. This period was characterized by extreme sensitivity to emotions of nurses ; impatience and an unsympathetic atmosphere could make a restless case almost maniacal. These cases all required gas-oxygen anæsthesia for actual delivery to control the inco-ordinated movements of the patient. Application of forceps was not required in any case. In all cases but two (women four days in labour) the child cried spontaneously. In all patients amnesia was complete from the time of the first dose of nembutal to waking up a few hours after labour.

(2) In shorter labours the dosage of nembutal was as follows : nembutal gr. vi was given, followed in one hour by syrup. chloral hydrate drachms ii. These cases received their nembutal within six hours of delivery ; they all rested quietly between pains, and were able to co-operate in the second stage of labour, so that additional anæsthesia was not required. All babies cried spontaneously at birth, and the placenta was expelled within fifteen minutes. Analgesia was more marked, and restlessness much less than in the first set of cases. Amnesia was not so complete and in some cases took twelve hours to develop.

The disadvantages of the technique of large doses of nembutal are that the patient cannot be left for more than a few minutes when restless, and that great attention must be paid to the emptying of the bladder.

The great advantage is that a woman mentally and physically exhausted by a long labour can be given a period of rest with safety, and is saved the memory of hours of distress.

Dr. N. F. MACLAGAN : The effects of anæsthetics (including barbiturates) on liver function in the normal animal have been investigated particularly by Rosenthal and Bourne (1928) and by Bourne, Bruger and Dreyer (1930). These workers used the blood bilirubin concentration and the bromsulphalein test as indices of liver function ; in the latter test 5 mgm. of the dye were injected intravenously and the residue determined in the plasma after fifteen minutes, at which time there should be none left in the normal animal. The main conclusions from this work were illustrated by charts and may be summarized as follows :—

(1) Chloroform produced much more liver damage than any other anæsthetic ; two hours' inhalation leaving effects which were still demonstrable five weeks later with the dye test.

(2) Nitrous oxide plus asphyxia was the next in order of severity. (Seven days required for recovery.)

(3) Sodium amytal and avertin both produced slight damage at twenty-four hours, recovered from in forty-eight hours.

(4) Nitrous oxide and ether were completely recovered from in twenty-four hours.

The effect of asphyxia deserves special notice, suggesting that this factor might be as important as some of those investigated by Prof. Cameron in the experiments which he has just described (cold, hæmorrhage, &c.).

My own few results have been obtained with pentothal, which does not appear to have been widely studied from this point of view. Gross liver damage is, however, given as a contra-indication to this anæsthetic by the makers, by Jarman and Abel (1936), Van den Post (1936), and Organe and Broad (1938), and in 1938 Vaizey described a case of toxic jaundice following and apparently due to pentothal administration. This was a woman aged 44, somewhat anæmic from piles, who was given 0·6 grm. pentothal before an operation for relief of these. Jaundice appeared at forty-eight hours, was maximal after ten days, and complete recovery was eventually noted.

By kind permission of the honorary surgeons and anæsthetists of Westminster Hospital, I have been able to determine the serum bilirubin and phosphatase in 25 cases twenty-four hours after the administration of various anæsthetics for operations unconnected with the liver. Thirteen of these were given pentothal in doses varying from 0·3 to 0·8 grm., followed in some cases by gas and oxygen or ether. Two of these 13 showed abnormally high values (2·0 and 1·6 mgm. bilirubin per 100 c.c.) and repeat estimations on these two patients after a further three days gave normal results, leaving little doubt that this slight degree of latent jaundice was due to the anæsthetic. The results for phosphatase were all within normal limits and none of the other anæsthetics—which included avertin, ether, nembutal, and chloroform—gave abnormal figures.

This small series suggests that pentothal does have a deleterious effect upon the normal human liver in a small proportion of cases, but the degree of impairment is slight and recovery appears to be rapid.

The best test for detecting impairment of liver function before anæsthesia is at present a matter of opinion. The serum bilirubin may be estimated, and the bromsulphalein test is merely a refinement of this, as the dye is excreted in the bile and it is therefore a test of excretory function. The galactose tolerance test offers an opportunity of testing a function which is independent of excretion and may be of more value. For this test it is desirable to estimate the blood-galactose, and not the total blood-sugar.

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Dr. H. J. Brennan: A patient under a normal depth of avertin or barbiturate narcosis can be aroused instantly by the intravenous injection of 8, 10, or 12 c.c. of coramine; and while such treatment is not to be recommended as a routine, the knowledge that one can arouse these patients if necessary is valuable. I have given evipan to over 1,000 patients who were being treated with radium for carcinoma of the cervix, the patient being in the knee-chest position. Nearly all of them had previously received more than a sterilizing dose of X-ray radiation and I have been struck by the greater relaxation and longer recovery period obtaining in these patients as compared with others. This observation becomes all the more interesting in view of Professor Cameron's findings in castrated female rats.

Section for the Study of Disease in Children

President—E. A. COCKAYNE, D.M.

(*November* 25, 1938)

CASES

Multiple Epiphyseal Dysplasia.—D. E. YARROW, M.B. (for the PRESIDENT). Boy, aged 7 years.

Birth-weight 7½ lb. Has always been undersized for his age. For two years has had occasional pains in lower limbs; during this period thyroid treatment has made no improvement. Poor appetite.

Family history.—Two other children alive and well. No similar condition in family. No consanguinity of parents.

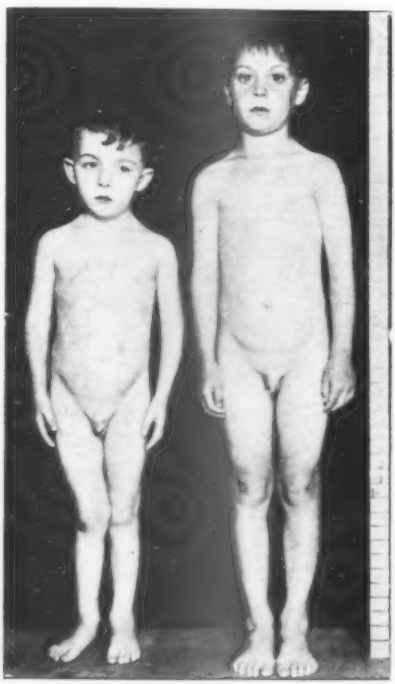
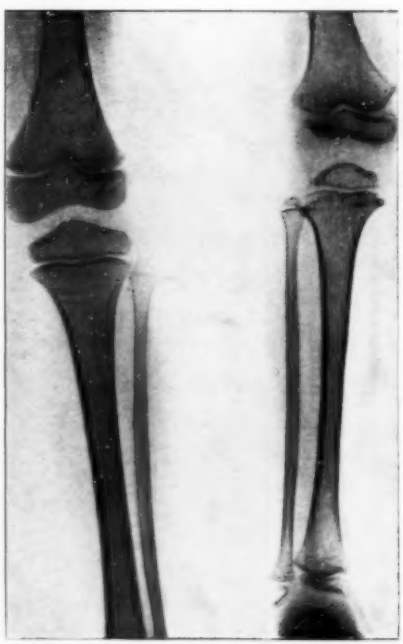


Fig. 1.—August, 1938



Control. Fig. 2.

On examination (6.9.38).—Undersized but normally proportioned and healthy in appearance. Height 39¼ in. (standard 46 in.). Weight 28 lb. (standard 49 lb.). No evidence of rickets. Genu valgum with 1½ in. separation at ankles. Peculiar gait (fig. 1).

X-ray photographs (with control) show: Skull: No abnormality. Long bones: General decalcification, especially in diaphyses, and deformed stippled epiphyses with delayed growth. Irregularity and interference with growing ends of all long bones (fig. 2). Similar changes in ossific centres in carpus, tarsus, and spinal vertebræ.

Enchondral, endosteal and periosteal bone formation are all affected.

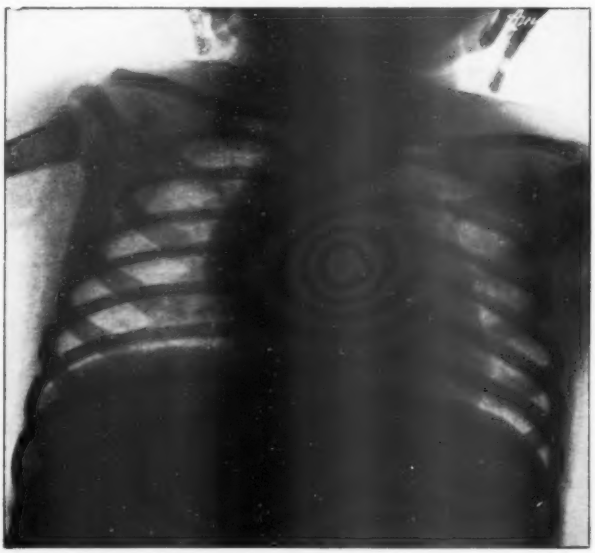
Further investigations.—Urine: Normal. Serum calcium 10·7 mgm.%; plasma phosphorus 4·0 mgm.%; plasma phosphatase 9·7 units. Blood urea 25 mgm.%. Fæcal fat: Total 6·7%; 7·6% split. Wassermann reaction negative.

The PRESIDENT said the case did not fall into any of the recognized groups. Mr. H. A. T. Fairbank had seen it and agreed with this statement.

Cardiomegaly in an Infant: Idiopathic.—REGINALD LIGHTWOOD, M.D., and DONALD COURT, M.B., M.R.C.P.

A. V., female, aged 9 months.

History.—A full-time infant of normal appearance and development at birth, who has gained weight and thrived satisfactorily up to the present time. During the first week of life she was thought to have a bad cold, and a cough developed. Brought to hospital at the age of 4 months on account of the cough, which had continued throughout the intervening period. At that time clinical examination showed a slight enlargement of the heart, and this was confirmed radiologically. X-rays showed enlargement of generalized type and the trachea deviated slightly to the right.



Cardiomegaly in an infant: Note generalized cardiac enlargement and deviation trachea to the right.

Bronchial breathing could be heard over a small area below the inner third of the right clavicle. No cardiac bruit has been heard.

The progress of this patient has been followed and the size of the heart has been estimated at intervals. The radiograms show that the cardiomegaly has been increasing. She has progressed well and has no symptoms except cough.

In order to see if the cardiomegaly was due to vitamin-B deficiency, marmite was given over a period of three months.

To ascertain if there was evidence of abnormal glycogen storage an adrenalin test was carried out. Normal results were obtained.

Hours after adrenalin	Fasting	¼	½	¾	1
Blood sugar % ..	0·085	0·116	0·173	0·190	0·186

No enlargement of liver. No ketone bodies in urine.

Blood-count (October 18, 1938): R.B.C. 5,920,000; Hb. 76%; C.I. 0·6.

Comment.—The picture is that of an apparently normal child of 9 months presenting clinical and radiological evidence of cardiac enlargement. The question at issue clearly concerns the underlying pathology. In attempting to establish this the following conditions were considered.

(1) *A combination of congenital cardiac lesions.*—There were several points against this diagnosis: the child was normally developed; finger-clubbing and cyanosis were absent. The heart sounds were not altered, nor were there any additional characteristic murmurs.

(2) *Avitaminosis B.*—Beri-beri in children is practically unknown in this country. Furthermore, there were no other features of this condition present and three months' treatment with vitamin B, as marmite, produced no effect on the cardiac enlargement.

(3) *Glycogen storage disease.*—This was excluded by the normal development, absence of hepatomegaly and ketonuria, and normal blood-sugar response to adrenalin.

(4) *Congenital idiopathic hypertrophy.*—This condition has recently been reviewed in the literature and six more cases added by Kugel and Stoloff. They show that the picture is essentially a composite one and the ultimate allocation of any case to this group can only be made by autopsy and careful serial histological section of the heart muscle. Clinically they stress the following points:—

(*a*) Over half the cases occur in the first year of life.

(*b*) The onset may be insidious with anorexia and irritability. More usually it is acute, a previously well child presenting cyanosis, dyspnœa, vomiting, and collapse.

(*c*) Gross cardiac enlargement, in which all chambers are involved but mainly the right side.

(*d*) It runs an afebrile course and a fatal termination occurs within from three days to three weeks.

The pathology in the cases reviewed included some with glycogen storage and others with major congenital defects. The majority, however, presented either pure hypertrophy of the cardiac muscles—this was the smaller number—or hypertrophy with areas of atrophy—replacement fibrosis and lymphocytic infiltration. In many cases some degree of pulmonary atelectasis was present as well.

Postscript (2.2.39).—The patient has remained in good health, and after a period of three months skiagrams show that the cardiomegaly is regressive.—R. L.

Reference.—Kugel and Stoloff, 1933, *Am. Journ. Dis. Child.*, **45**, 828.

Discussion.—The President did not think congenital malformation could be ruled out even in spite of the absence of murmurs and cyanosis.

Dr. F. Parkes Weber said he did not think that glycogen-storage disease could be excluded as a possible explanation of the cardiomegaly, as apart from that finding the child appeared healthy.

Dr. Herbert Levy quoted a case of idiopathic cardiac hypertrophy reported by Doxiades (Report of Meeting, Berlin Pædiatric Society, 20.5.38; *Klin. Wschr.*, **17**, 1526). The child

had developed signs of circulatory insufficiency fifteen days after birth and had died seven days later. On autopsy considerable hypertrophy of the heart, especially of the right ventricle, was found (weight of heart : 65 grm.) ; no valvular lesion ; no glycogen storage of the heart muscle. With regard to Dr. Parkes Weber's question as to the significance of vitamin B_1 in such a case : cardiac enlargement is nearly always present in beri-beri owing, as shown by Wenkebach, to an œdematous swelling of the muscle fibres.

Dr. W. M. FELDMAN thought that the case was not one of congenital heart disease without a murmur, as such cases are generally of the cyanotic type. He thought it might be a case of idiopathic cardiac hypertrophy.

Dr. HELEN MACKAY reminded the Section of one possible cause of cardiomegaly in an infant without murmurs and without cyanosis, which had not been mentioned, namely tuberose sclerosis associated with rhabdomyomata, an example of which had been shown at a meeting of this Section by Dr. E. O'Flynn and herself last year.[1] There was, however, nothing to suggest this was a likely diagnosis in Dr. Court's case.

Congenital Air-containing Cysts of Lung.—R. S. ILLINGWORTH, M.D. (by courtesy of Dr. DONALD PATERSON).

Girl, aged 1 year and 6 months.

Family history.—Nothing of note. No history of tuberculosis.

Present complaint.—The child was brought to the Out-patient Department of the Hospital for Sick Children, Great Ormond Street, on August 2, 1938, on account of symptoms suggestive of masturbation, dating from an attack of bronchitis in the preceding January.

Previous history.—Normal delivery, three weeks before term ; birth-weight 6½ lb. Breast-fed till 11 months ; there was always some difficulty in persuading the

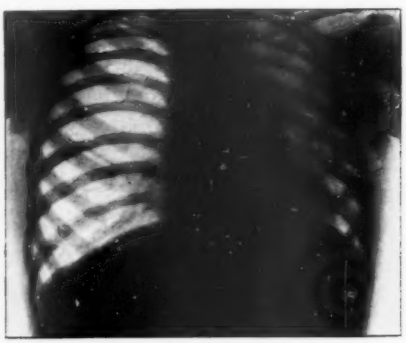


Fig. 1.—30.8.38

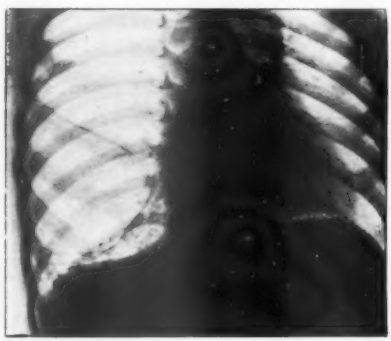


Fig. 2.—5.9.38.

child to take enough food, and gain of weight was slow. Milestones in development all passed at the normal time.

There has been an intermittent cough since birth. In January 1938 she had an attack of bronchitis and laryngitis, lasting for three weeks, associated with a severe cough, with some vomiting, and two attacks of cyanosis in bouts of coughing. There has been no other history of cyanosis before or since this time.

Since January the cough has diminished, and apart from masturbation the child has been perfectly well and healthy.

On examination.—Well-looking intelligent child. Decreased breath sounds, and

[1] *Proceedings*, **30**, 1063 (Sect. Dis. in Child., 47).

hyper-resonance on right side of chest. Heart displaced to left; apex beat palpated in 4th space outside nipple line.

Skiagrams of chest: Displacement of mediastinum to left. Marked translucency on right side. Markings on right suggesting a loculated air-containing cyst of lung (figs. 1 and 2).

Paracentesis (thoracic) showed positive pressure; 100 c.c. of air were withdrawn, and a further 70 c.c. on the next day: the pressure was then still positive.

Bronchography: Apparently normal filling of left bronchial tree with partial filling of right lower lobe bronchi; large cyst at right base not entered by lipiodol.

Bronchoscopy (Mr. James Crooks): There was a marked narrowing of the right main bronchus 2 in. from the bifurcation, but no signs which suggested that this was a post-inflammatory condition; it was thought to be congenital.

Blood-count normal. Urine normal. Sedimentation rate normal.

Mantoux test: 1 : 1,000 and 1 : 100 negative.

Pulse and temperature were normal while the patient was in the ward.

Respiration rate: 22–30.

Progress.—Physical signs and radiographs showed no change in the child's condition during her stay in hospital, and the signs were present when she subsequently attended the Out-patient Department on 11.10.38.

Congenital Steatorrhœa with Congenital Morbus Cordis.—C. HARDWICK (by permission of Dr. W. J. PEARSON).

D. R., male, aged 5 years 6 months, was seen at the Hospital for Sick Children, Great Ormond Street, on account of persistent diarrhœa which had been noticed since the age of 2 years. The bowels were being opened from six to seven times a day and the motions were large, pale, and greasy, and at times oily drops were passed. His appetite was very big.

History.—The patient is the elder of two children, born of healthy unrelated parents. No family history of any similar disease. Born at full term, weighing 7½ lb.; breast-fed for seven months. An attempt to wean him at this time caused digestive upset and breast feeding was continued until 9 months. He was then given dilute milk mixtures and was not able to take whole milk until he was 18 months old. At the age of 2 years the frequent large motions were first noticed. He has had measles and frequent attacks of tonsillitis. He has not had bronchopneumonia.

On examination.—A thin boy with a high colour and somewhat distended abdomen. No wasting of buttocks, no signs of rickets. Weight 31 lb. (standard 47 lb.). Height 42¼ in. (standard 45 in.). Respiratory system: Normal. Cardiovascular system: Apex beat 4th space in nipple line, no thrills; systolic murmur maximal at apex; clubbing of fingers. Abdomen: Distended; nothing palpable. Central nervous system: Normal.

Investigations

Stools:—

	26.9.38	7.10.38	11.10.38
Split fat	45·06%	18·16%	21·66%
Unsplit fat	18·89%	22·69%	15·14%
Total fat	63·95%	40·85%	36·80%
or, of the fæcal fat:			
	70·5% is split,	44·5% is split,	58·9% is split,
	29·5% is unsplit.	55·5% is unsplit.	41·1% is unsplit.
Microscopically	Fat globules and muscle fibres.	A few fat globules and undigested meat fibres.	Excess of fat globules and undigested meat fibres and unabsorbed starch.

Urine: Sterile. Diastatic index 10 units (normal).

Blood analysis: Calcium 7·5 mgm. per 100 c.c. serum; inorganic phosphorus 3·7 mgm. per 100 c.c. whole blood; plasma phosphatase 7·8 units.

Glucose tolerance curve:—

Hours after 19 grm. dextrose	0	½	1	1½	2	3
Blood-sugar %	0·076	0·109	0·122	0·128	0·142	0·078

Urine: No sugar.

Loewi's test: Negative.

Blood-count: R.B.C. 4,420,000: Hb. 90%; C.I. 1·0.

Sedimentation rate: 8 mm. in 1 hour (normal).

Mantoux test (1 : 1,000): Negative.

Skiagrams: Wrist: Normal ossification, no decalcification. Chest: Cardiac shadow normal, increase of hilar shadows.

Discussion.—The PRESIDENT agreed with the diagnosis. He had read the recent papers by Harper and Andersen and thought that cystic fibrosis of the pancreas was the same as congenital steatorrhœa. Andersen had found that almost all the acinar tissue was absent. The cysts, when present, appeared to be secondary. The condition, judging by the familial incidence and the high rate of consanguinity in parents, was recessive, but the recent papers unfortunately did not add to our knowledge on this point.

Dr. PARKES WEBER said that Dr. K. Fürth had investigated and described this condition in a case at the German Hospital. The patient was one of two sibs who afterwards attracted the attention of Sir Archibald E. Garrod, who had published the earliest report of this disease. Dr. Weber was anxious to know whether the prognosis as to the duration of life was really so bad in these cases.

Dr. W. M. FELDMAN thought that in view of fact that in congenital morbus cordis there is generally a polycythæmia, the normal blood-count in this case may indicate a relative oligocythæmia. He therefore suggested that the average diameter of the red cells be measured. A macrocytosis might explain the steatorrhœa.

Albers-Schönberg Disease. An Atypical Case.—C. ELAINE FIELD, M.D. (by courtesy of Dr. DONALD PATERSON).

In May 1934, Edward L. and his brother Derek L. were shown at this Section by Ellis as two cases of osteopetrosis with certain atypical features representing a familial variation. Since then these atypical features have become accentuated and, with added neurological signs, throw some doubt on the diagnosis. Edward L. is now 6 years of age, and his brother 7½ years.

Family history.—The parents are second cousins and, from skiagrams of their right hands, show no evidence of bony dystrophy. The elder brother, Derek L., is now bedridden suffering from osteopetrosis of almost identical type with that seen in Edward L.

History of Edward L.—A full-term child, forceps delivery, weighing 8½ lb. at birth. Sat up at 13 months and stood at 17 months. In May 1934, at 18 months, he was admitted to the Hospital for Sick Children with tonsillitis, and the skeletal deformities were noticed. At this time the external appearances and X-ray pictures showed a less advanced degree of the present condition. Internal strabismus and optic atrophy were present, but no other abnormal physical signs in the nervous system were detected apart from hydrocephalus. In 1935 his tonsils and adenoids were removed. Until three months ago he was able to run about, but since then he has complained of tiredness after walking, and loss of balance has gradually increased.

Investigations May 1934 (Dr. D. Nabarro).

Blood-count: R.B.C. 4,200,000; Hb. 62%; C.I. 0·73; W.B.C. 14,000. Serum calcium, inorganic blood-phosphorus, plasma phosphatase, blood-urea, and cholesterol, were within normal limits. Blood Wassermann reaction negative (14.5.34).

Present condition.—Unable to stand without support but able to feed himself. Skull: High with bossing of frontal and parietal bones. Eyes prominent, bilateral weakness of the external rectus muscles. Marked pigeon-chest deformity and expansion of the ends of the long bones. No enlargement of liver or spleen. There is a faint bluish mottling of the skin over the front of the chest and upper part of the abdomen first noticed in October 1938, resembling the macular atrophy observed on his brother four years previously (fig. 1).

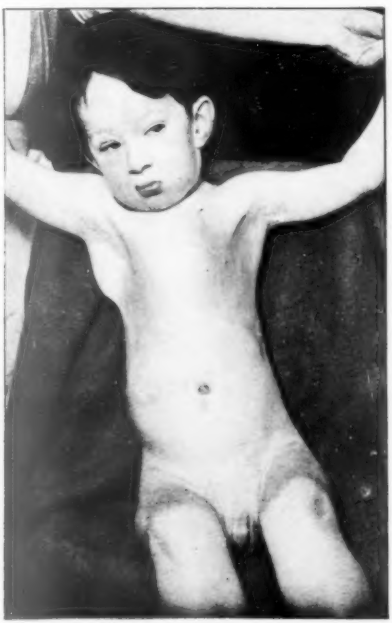


Fig. 1.—E.L.

Nervous system: Mentally slow. Optic atrophy with bilateral blindness (perception of light and form only). Deep reflexes of legs exaggerated, and bilateral extensor plantar responses.

Cerebrospinal fluid: Clear, colourless, without clot formation, and sterile. Pressure normal. Queckenstedt's test positive. Cells, 35 per c.mm. (86% mononuclear cells, 14% polymorphs). Total protein 30 mgm. per 100 c.c., and no increase in globulin. Lange gold curve 0000000000. No evidence of lymphocytic choriomeningitis on injection of cerebrospinal fluid into mice and guinea-pigs.

Blood-count: R.B.C. 4,240,000; Hb. 85%; C.I. 1·0; W.B.C. 7,600. Polys. 59%; lymphos. 37%; monos. 3%; basos. 1%. Platelets 350,000. Reticulocytes 1%.

Skiagrams (figs. 2, 3, 4 and 5).

Skull: Enlarged cranial vault with increased density of bone most marked at the base. Long bones: tibia, fibula, femur, humerus, radius, and ulna. Marked increase of cortical bone at the centre of the shaft only. Expansion of the ends of the bones with transverse striations of increased density. Stippling of the epiphyses. Pelvis: Patchy symmetrical increased density of bone with a circular stippled area over each

Fig. 2.—Enlarged cranial vault with increased density of bone most marked at the base.

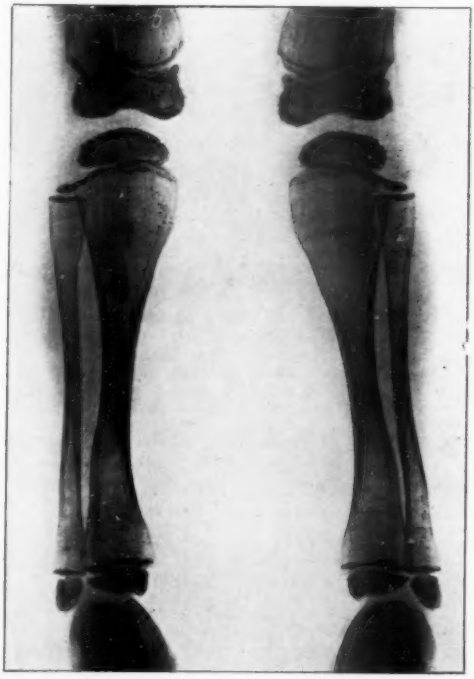


Fig. 3.—Tibiæ and fibulæ. Marked increase of cortical bone at the centre of the shaft only. Expansion of the ends of the bones with transverse striations of increased density. Stippling of the epiphyses.

Fig. 4.—Vertebral bodies flattened, with wide intervertebral discs. The anterior parts taper to a crescent-shaped surface.

acetabulum. Ribs: Normal. Vertebral bodies: Flattened, with wide intervertebral discs. The anterior parts tapering to a crescent-shaped surface.

Commentary.—This case shows many characteristic features of Albers-Schönberg disease: Osteopetrosis of the skull, long bones, and pelvis, with clubbing of the metaphyses and transverse striations of increased density; hydrocephalus with primary optic atrophy and VIth nerve palsy; familial history and parental consanguinity. But the unusual distribution of the osteopetrosis, the stippling of the epiphyses, the changes found in the vertebral column, absence of anæmia, no enlarge-

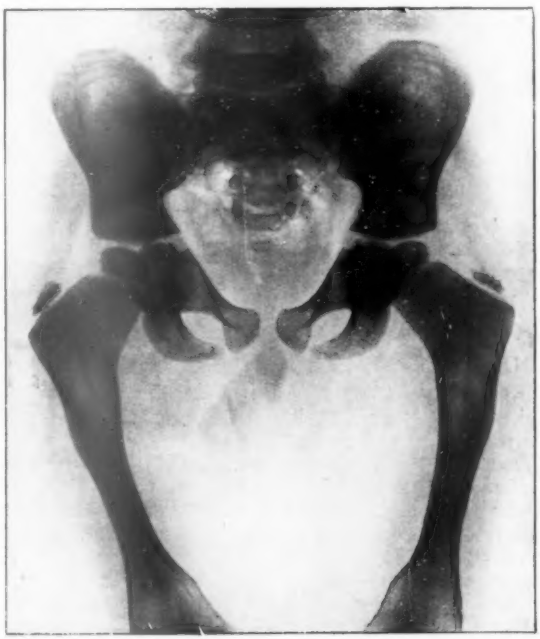


Fig. 5.—Pelvis. Patchy symmetrical increased density of bone with a circular stippled area over each acetabulum.

ment of liver or spleen, mottling of the skin, and the neurological signs, combine to make this an atypical case.

The brother, Derek L., was admitted to hospital in January 1938 following a convulsion. No abnormal physical signs were detected in the nervous system apart from the optic atrophy and VIth nerve paresis noted in 1934.

The cerebrospinal fluid contained 15 cells per c.mm., but was otherwise normal. Nevertheless the skeletal abnormalities, as shown by X-rays, were almost identical with those of his brother: the liver and spleen were not enlarged, the blood-count was normal, and he also shows macular atrophy of the skin of chest and abdomen.

As suggested by Ellis, these two cases probably represent a familial variation of the original Albers-Schönberg disease.

Reference.—Ellis, R. W. B. (1934), *Proc. Roy. Soc. Med.*, **27**, 1565 (Sect. Dis. in Child., 67).

Discussion.—The PRESIDENT said he thought the condition in the two brothers was Albers-Schönberg disease, though in some respects atypical. In shape, though not in density, the long bones were typical. Such thick bone at the base of the skull causing optic atrophy was unknown in any other condition. Both brothers had the same deformity of the chest, which had not been described before, and both had small circular areas of atrophic skin over the trunk, which had never been described in association with marble bones. He had tried in vain to persuade the mother to agree to a biopsy. Nussey had recently shown by the high rate of first-cousin marriages in the parents that Albers-Schönberg was recessive, and these boys were children of second cousins. This was another point in favour of the diagnosis. Dr. Batten recently showed lantern slides of the bones of the boys and said he thought they had atypical osteogenesis imperfecta, a condition with which the speaker thought they had nothing in common.

Dr. R. W. B. ELLIS said he was particularly interested to see this case four years after having shown the two brothers before the Section (May 1934), as since that time several authorities had questioned whether they should really be regarded as examples of Albers-Schönberg disease. Personally, he was still inclined to agree with the President that the similarities with other cases, e.g. the deposition of densely calcified bone at base of the skull, optic atrophy, &c., justified their inclusion as familial variants within this group. The areas of dense stippling which were now appearing had also been described in other cases of marble bones. In view of the many atypical features such as the site of the cortical thickening in the centre rather than at the ends of the long bones, it might be well to differentiate them as " Type L " (from the family initial). The present X-rays definitely gave the impression of showing areas of *rarefaction* as compared with the earlier ones. If a parathyroid origin of the disease were proved, it might be that these and the dense areas were due to different phases of activity. In any case, the whole clinical picture did not appear to correspond closely with any other syndrome previously described.

Two Cases of Diabetes Mellitus with Gross Hepatomegaly and Jaundice.—S. D. M. COURT, M.B., M.R.C.P. (by courtesy of Dr. DONALD PATERSON).

I. Male child, aged 10 years. A known diabetic for four years, treated with restricted carbohydrate diet and soluble insulin, 10 units twice daily.

History of present phase (31.5.38).—Admitted to Hospital for Sick Children. Three weeks before admission he had an illness characterized by diarrhœa and vomiting. On the third day jaundice appeared, of an obstructive type, which reached its zenith in one week and then slowly receded. Lens opacities in both eyes of diabetic type.

Examination on admission.—Height 48¾ in. Weight 52¼ lb. Jaundice still present. Gross hepatic enlargement, lower edge below the umbilicus; firm consistency, smooth surface. No splenomegaly. No evidence of ascites but superficial abdominal veins prominent.

Special investigations.—31.5.38 : Urine : Glycosuria and ketonuria ; sterile ; no bile salts or pigments. Fasting blood-sugar 474 mgm.%. Van den Bergh reaction : " Biphasic " indirect reaction. 2 units of bilirubin. Sedimentation rate : 43. Mantoux test 1 : 1,000 +. Wassermann reaction negative. Galactose tolerance test revealed defective liver function. Takata's test for cirrhosis positive.

Fæcal fats : 7·05% dried fæces ; 55·2% split ; 44·8% unsplit.

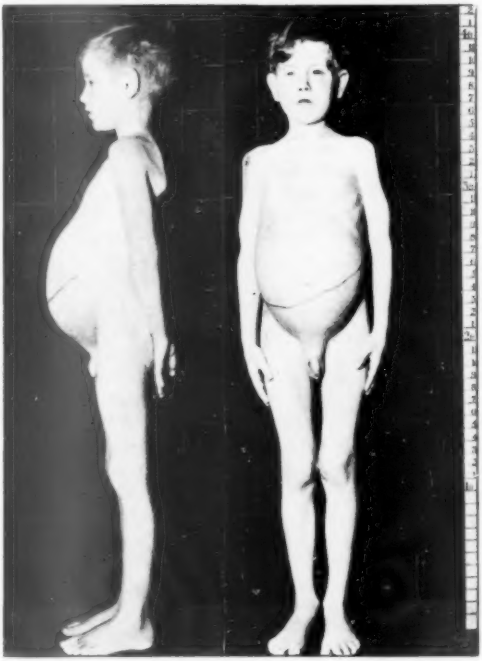
Blood-cholesterol—31.5.38 : 340 mgm.% ; 20.6.38 : Cholesterol 218 mgm.%.

Blood : Total fatty acids and phospholipin phosphorus, normal. R.B.C. 5,080,000 ; Hb. 106% ; C.I. 1·06. Fragility of red corpuscles : Complete hæmolysis in 0·33% salt solution. Trace in 0·42%. Diastatic index of urine : 2 units.

15.7.38 : Discharged. Diabetes controlled with (1) diet containing 200 grm. carbohydrate, (2) soluble insulin 66 units daily. Jaundice had now disappeared and liver was receding slowly, being above the umbilicus.

Past health.—Known diabetic for four years prior to admission. No previous history of jaundice. Parental story of intermittent abdominal swelling for two years.

Subsequent history.—29.8.38 : Child readmitted. Diabetes again uncontrolled, with fasting blood-sugar of 500 mgm.%. Abdomen larger than ever and liver edge below the umbilicus. Control was established with the same insulin dosage.



Case 1.

9.9.38 : Admitted to convalescent home. At the end of September albuminuria (100 mgm.%) developed : evidence of free fluid in the abdomen. By 15.10.38 these symptoms had disappeared.

28.10.38 : Hypoglycæmic coma.

11.11.38 : Readmitted to hospital. Liver still enlarged just above the umbilicus. Glycosuria and ketonuria. Fasting blood-sugar 250 mgm.%.

Treatment.—(1) High carbohydrate diet ; (2) insulin ; (3) special pancreatic abstract has been given for two months ; (4) campolon.

II. Female child, aged 5 years.

27.6.38 : Admitted to Hospital for Sick Children.

History of present complaint.—Vague ill-health for one year. Three months before admission insidious onset of jaundice which developed for three weeks and then slowly declined but never completely cleared. Polyuria, polydipsia, pruritus, and loss of weight for two weeks.

Past health.—No previous jaundice.

Family health.—No history of jaundice or diabetes mellitus.

On examination.—Moderately well nourished. Rather dark skin. Very drowsy. Marked glycosuria and ketonuria. Fasting blood-sugar 428 mgm.%.

Abdomen: Small umbilical hernia. Liver enlarged, lower edge just above the umbilicus; firm consistency. Spleen just palpable. Fundi and media normal.

Special investigations.—Wassermann reaction negative. Takata's test negative. Mantoux 1 : 1,000 negative. Urine: No bile pigments; sterile. Van den Bergh direct reaction biphasic, indirect 1·5 units. 11.7.38: Indirect 5·5 units. 20.7.38: Indirect 2·5 units. Galactose tolerance test normal.

Cholesterol: 460 mgm.%. 9.9.38: 105 mgm.%.

Fæcal fat: Total 20·75%; 85% split.

Blood-count, 27.6.38: R.B.C. 5,540,000; Hb. 56%; C.I. 0·5; W.B.C. 10,300. 15.11.38: R.B.C. 4,640,000; Hb. 78%; C.I. 0·8; W.B.C. 13,700. Eosinophiles: 27.6.38, 35%; 11.7.38, 20%; 27.7.38, 25%; 9.9.38, 32%; 15.11.38, 23%. No parental eosinophilia.

Fragility of red corpuscles: Both child and parents normal. Sedimentation rate 15.

No parasitic ova or worms seen at any time in fæces.

Casoni test: Negative.

Urinary diastase 8 units.

Present position.—Diabetes controlled with: (1) High carbohydrate diet. (2) Insulin—10 units twice daily at first, now protamine zinc insulin, one injection daily.

Liver has decreased in size but is still two fingerbreadths below costal margin. General condition excellent.

Comment.—Those cases draw attention to a syndrome occurring in juvenile diabetes which has up to the present received but scant attention in medical records. The main features are as follows:—

(1) *Diabetes mellitus.*—This is severe—of early onset and considerable duration—difficult to control. Hanssen, reviewing a two-and-a-half-year period, noticed twelve examples in 44 patients below the age of 20 and only one in 231 over that age. The average duration of the disease was four years.

(2) *Enlargement of the liver.*—The lower edge may vary in position from 2 to 5 in. below the costal margin in the midclavicular line. The surface is smooth—the consistency rather soft, and the organ as a whole is not tender.

(3) *Jaundice.*—This is not invariable. It did not occur in any of Hanssen's cases. It was present in both the cases under consideration. In three cases reported by Grayzel and Radwin it occurred on several occasions. It resembles typical infective hepatitis and, as the latter authors point out, it is not the cause of the hepatomegaly, though the latter probably renders the patient more susceptible.

(4) *Nutrition.*—Good—the stature and weight are normal or just below normal.

(5) *Blood chemistry.*—(*a*) Fasting blood-sugar never below 300 mgm. before adequate treatment instituted. (*b*) High initial blood-cholesterol. (*c*) High total lipoids.

The present cases.—Case I clearly belongs to the syndrome described. The pathology is difficult to assess. The failure to respond to either insulin or insulin with pancreatic extract points to this being either a case of glycogen storage disease in which diabetes has supervened, or fatty infiltration followed by cirrhosis. The persistent enlargement, the prominence of the superficial abdominal veins—the recent ascites and the positive test point to the latter conclusion.

Case II is rather more controversial. It is open to question whether she really belongs to the syndrome outlined above. Here the jaundice preceded the diabetes. The latter is of moderate severity and easily controlled. The liver is very firm and the spleen enlarged. This may be simply a case of diabetes mellitus arising during the protracted course of an infective hepatitis which has later progressed to subacute hepatic necrosis. The latter process presumably is now arrested. No explanation is offered for the marked and persistent eosinophilia. The clinical picture bears only

superficial resemblance to the cases described by A. P. Thomson, Haswell Wilson and Stuart McDonald, in which jaundice, hepatomegaly, and a high eosinophilia were present and attributed to a condition akin to tularæmia.

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Prognosis and treatment.—There are three main groups: (1) Adequate control of the diabetic state by which relatively large doses of insulin are required; this produces regression of the liver in the majority of cases. In Hanssen's series all returned to normal within a period of seventeen weeks.

(2) This is a combination of Group I with the addition of alcoholic extract of beef pancreas. Three to five months were required to produce full hepatic recession: enlargement returned if the pancreatic medication was discontinued. The active factor in the pancreatic extract is not lecithine or choline but some other factor. The three cases reported by Grayzel and Radwin belong to this group.

(3) There is little or no response to treatment in this group.

Pathology.—Pathological findings are not uniform. Hanssen postulated a fatty infiltration because of the ease of regression with adequate diabetic control—the results of animal experimentation and the human autopsy findings in three cases reported by White. These would seem to correspond to Group I in treatment.

Stetson and Ohler in liver biopsy from a typical case, and Brian, Schechter and Persons in an autopsy, report the paradoxical presence of an enlarged liver containing an excessive amount of glycogen in a patient with severe ketosis.

No congestion, cirrhosis, or hæmochromatosis, was found in the latter case. They suggest that the mechanism here was either (1) diabetes mellitus supervening in a patient with glycogen-storage disease (two cases reported by Gjurik support this), and (2) the excessive storage of glycogen under the influence of insulin. In some of the cases which are refractory to treatment the presence of hepatic cirrhosis is presumed.

Discussion.—Dr. PARKES WEBER alluded to a type of splenomegaly with large clear cells (? containing cholesterol) having been found in certain rare cases of diabetes mellitus. He suggested that the enlargement of the liver and jaundice in one or both of the present cases might be due to biliary obstruction, in some respects analogous to that in so-called Hanot's cirrhosis, but due to cholesterol deposit in the small biliary ducts. Such visceral cholesterol deposits might be compared to those in the skin in the various types of diabetic xanthoma.

Dr. R. D. LAWRENCE said that he had seen hepatomegaly in many diabetic children, extreme in a few cases. This he had put down to the high degree of lipæmia and disordered fat metabolism always found in his cases. The enlargement had always gradually disappeared when the fat metabolism was put right by liberal carbohydrate and adequate insulin to metabolize it.

He suggested that in Case I there had not been a prolonged enough period of adequate diabetic control to allow the liver to go down.

In Case II he suggested that the unexplained high eosinophilia might be due to the insulin injections as he had observed this in a series of cases published in 1929.

Two Cases of Anaphylactoid (Henoch-Schönlein) Purpura.—DONALD BATEMAN, B.M., M.R.C.P. (by permission of Dr. A. G. MAITLAND-JONES).

I.—R. P., male, aged 5 years.

8.7.37: Admitted to London Hospital because of abdominal pain.

Present illness.—Nineteen days ago attack of severe abdominal pain. No fever. Bowels normal. No vomiting. Since then repeated attacks of abdominal pain, often

doubling him up. Getting milder. Fourteen and seven days ago passed a little blood in watery motions. Motions have been more or less regular. Good deal of tenesmus. No fever or vomiting. Lethargic. Almost complete loss of appetite. Day before admission had pain in left side of head. On day of admission swelling of forehead appeared.

Family history.—Parents and three siblings, all well.

Past history.—Whooping-cough. Tonsillitis.

On examination.—Temperature 98° F. Respirations 28. Pulse 96. Thin, ill, wasted, and with dry skin. Fretful. Diffuse pitting, œdematous swelling of forehead, most marked at root of nose. No inflammation of skin in this area. Tonsils enlarged and slightly inflamed. Tonsil glands slightly enlarged. Other glands normal.

Central nervous system: No evidence of meningitis. Difficulty in obtaining knee- and ankle-jerks. Normal in all other respects. Optic fundi normal.

Heart normal. Lungs normal. Ear-drums normal.

Abdomen: Thin-walled. Visible peristalsis of small intestine, with ladder-pattern. No rigidity or real tenderness. *Per rectum:* No blood (but some was present in motion shortly afterwards). Small, soft lump felt on anterior rectal wall.

Urine normal.

Mantoux test 1 : 1,000, negative.

9.7.37: Purpuric spots appeared on both elbows. Proctoscopy (Mr. Charles Donald) revealed a small globular mass, ½ in. in diameter, with small superficial ulcer, on anterior rectal wall. Small piece of mass removed for pathological study. Report: "Fibrino-muco-purulent catarrhal membranous proctitis" (Dr. W. W. Woods).

10.7.37: Seven motions all containing blood. Purpuric eruption on buttocks. Rectal swab: "No pathogenic organisms grown." Throat swab: "Predominant organisms, pneumococci, streptococci, and a yeast."

Patient continued to have frequent bouts of severe abdominal pain, but they gradually decreased in severity and became less frequent. There were occasional bouts of diarrhœa.

21.7.37: Had gross hæmaturia lasting one day only.

22.7.37: Passed 10 blood-stained stools.

25.7.37: One projectile vomit. Still had frequent blood-stained stools.

27.7.37: Sigmoidoscopy: "Appearances consistent with diagnosis of mild colitis and proctitis."

From then onwards steadily improved and gained weight.

19.8.37: Sigmoidoscopy: "Normal rectum."

22.8.37: Slight fever. Pain in left knee and right ankle. Left knee showed no abnormal physical signs. Right ankle showed slight urticarial and purpuric eruptions.

25.8.37: Left ankle swollen and showing urticarial and purpuric eruptions.

26.8.37: Slight abdominal pain. No fever. Albumin and occasional red and white cells in the urine.

During following week was fairly well.

1.9.37: Discharged from hospital as, though previously immunized to diphtheria, he was suspected of being a diphtheria carrier. During following two weeks was miserable and had pains in both knees accompanied by some swelling. Purpura on legs. No blood in stools or urine.

Since then has been perfectly well.

22.11.37: Perfectly normal in all respects. No physical abnormalities.

Blood Investigations

	R.B.C.	Hb.	W.B.C.	Polys.	Lymphos.
8.7.37			12,000	67%	28%
9.7.37	4,200,000	76%	12,000	77%	19%
	Platelets abundant. Bleeding-time 2½ minutes.				
12.7.37	3,200,000	68%	10,000		
	Platelets abundant. Bleeding-time 2½ minutes. Clotting-time 1 min. 50 secs.				
7.8.37	4,100,000	76%	6,000	26%	70%
	Platelets normal.				
26.8.37	4,600,000	80%	10,000	35%	58%
	Platelets 377,000.				

II.—K. H., aged 4 years.

18.11.38: Admitted to London Hospital because of abdominal pain.

Present illness.—Seven days ago rash appeared on both legs. Six days ago complained of abdominal pain; blood seen in stools. Two days ago vomited several times and passed several dark motions, described as of "reddish-brown" colour. Since then has continued to have severe, colicky abdominal pain at irregular intervals. Appetite very poor. Slight cough.

Family history.—Parents alive and well and have never had serious illness.

Past history.—Measles. Frequent bronchitis.

On examination.—Temperature 98·7° F. Respiration 32. Pulse 128. Pale, ill. Subcutaneous hæmorrhage of left eyelid. Slight gingivitis. Tonsils slightly inflamed. Tonsil glands enlarged. Other glands normal. No joint swellings.

Central nervous system: Normal. Optic fundi normal. Heart normal. Lungs: Small patch of diminished air-entry and medium crepitations over left lung base posteriorly.

Abdomen: Slightly distended. Resistant all over, most marked in upper half. No tenderness. Spleen just felt. Liver just felt. *Per rectum:* A little blood present on examining finger.

Urine: Trace of albumin. No blood.

Capillary resistance test: No change after three minutes' pressure on right arm.

19.11.38: Fresh crops of purpura on both arms. Large bruise on right arm where resistance test was carried out yesterday. Passed two normal motions.

20.11.38: Left elbow slightly swollen. Slight limitation of movement.

21.11.38: Intermittent colicky abdominal pain.

22.11.38: Profuse crop of purpura on buttocks. Abdominal pain continues in same manner. No fever.

Blood Investigations

	R.B.C.	Hb.	W.B.C.	Polys.	Lymphos.
19.11.38	3,800,000	72%	16,000	73%	21%
	Platelets 380,000. Bleeding-time 2 mins. 15 secs.				

Developmental Umbilical Abnormality.—W. M. MARTIN, M.D. (for Dr. JAMES CARVER).

H., male infant.

Born 13.10.38, weight 6 lb. 13 oz. Vigorous child. Pregnancy and labour had been normal; mother aged 35, stated to be a primipara. Apparently full-time pregnancy, menstrual history being doubtful.

The placenta and membranes appeared normal, but the cord, which was 20 in. in length, was grossly thickened. The thickening was generalized, but with fusiform deposits of Wharton's jelly which increased the diameter to 2 in. in parts. At the umbilical insertion the thickness was about 1½ in. The process of separation was unusually moist and was complete on the eleventh day. A raw stump slightly more than 2 in. long was left, having the appearance of granulation tissue and a brawny consistence.

There was no impulse when the infant cried, but palpation of the base of the stump suggested the presence of a core and that this process might be associated with

a Meckel's (or ileal) diverticulum. There has been no discharge except from the raw surface, some areas showing a superficial necrosis, and no evidence of any sinus. The appearance has altered little, except for a slight contraction of the process which has assumed a more bulbous form.

There is no attempt at epithelialization, the neighbouring skin being sharply demarcated. There have been no intestinal signs and progress has been almost uninterrupted. In spite of weaning the weight on 18.11.38 was 8 lb. 6 oz. (a gain of 25 oz. from birth-weight in thirty-six days).

Treatment.—The only treatment adopted was frequent packing in the standard type of powder cord dressing.

The case is shown as a developmental umbilical abnormality which is probably associated with the distal end of a Meckel's diverticulum, and in which sinus formation may ensue.

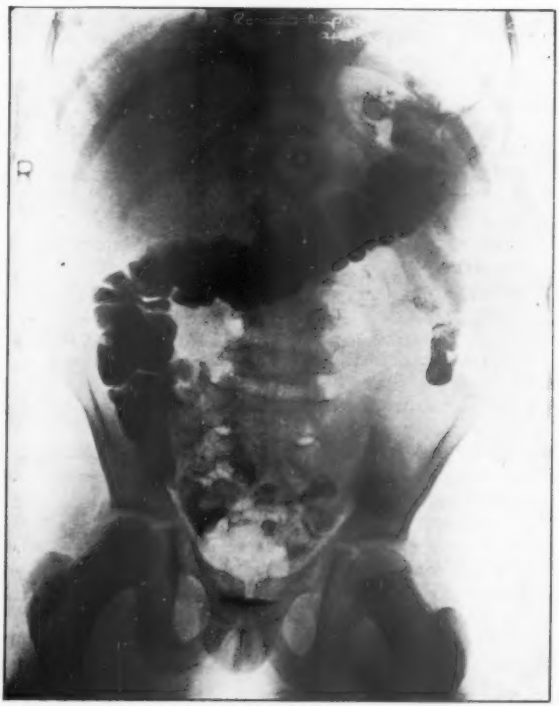
Mr. TWISTINGTON HIGGINS considered it probable that the condition was a partial exomphalos, undergoing absorption. He did not advocate operative intervention, at least for the present.

Hirschsprung's Disease, treated with Sympathectomy (Mr. T. Meyrick Thomas).—W. M. FELDMAN, F.R.C.P

Ronald N., aged 12 years.

Case shown November 26, 1937 (*Proceedings*, 31, 366, Sect. Dis. in Child., 22).

Skiagrams taken November 1938, fifteen months after the operation, show that the satisfactory result then obtained has continued.



November 1938. Skiagram showing normal haustration.

Section of Odontology

President—A. H. Parrott, O.B.E., M.D.S.Birm.

[*November* 28, 1938]

Radiological Findings in Some Less Common Jaw Affections

By H. M. Worth, M.R.C.S., L.D.S., D.M.R.E.(Camb.)

Certain specified affections of the jaw are considered, which are relatively rare and infrequently met with. Because of this their radiographic appearance is unfamiliar.

Sclerosing Osteitis

Most of us are familiar with the appearance of bone sclerosis at the apices of teeth, either in association with rarefying osteitis or occurring alone. It is also not infrequently encountered at the sides of apparently healthy teeth or sometimes surrounding and obscuring retained roots. It is generally regarded as being an infective process. What is not so well understood is that these areas of sclerosis may sometimes reach large size, so that some doubt is cast upon the radiographic interpretation (fig. 1). Apart from the greater extent of the sclerosed area, the

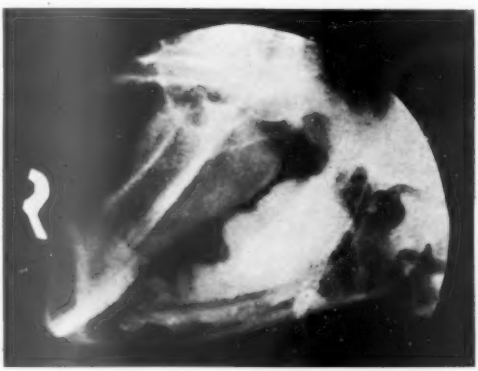


Fig. 1.—Massive sclerosing osteitis.

radiographic features resemble those of the small areas in that the bone structure is obscured by the filling in of the bone spaces by new bone, so that the whole involved portion is white in appearance and homogeneous in density. The margins tend to be more sharply defined than in the small areas. Those cases in which a large area is involved are rare and, in my experience, have occurred only in the mandible. They have been sent for radiographic examination on account of pain and, in one case, the pain was so severe that it had been considered necessary to operate upon the Gasserian ganglion. Fortunately, however, the local condition was recognized and excised, with complete relief of the symptoms. It is interesting to speculate on the ætiology of these large areas of bone sclerosis and it might be thought that they may follow osteomyelitis, but I have never found any evidence to suggest that such

was the case. Radiographically they have to be differentiated from : (1) *Composite odontome ;* (2) *osteitis fibrosa ;* (3) *osteoma.*

A *composite odontome* has a thin, dark line surrounding it which represents the site occupied by its fibrous capsule. Sclerosing osteitis is devoid of this capsule and is continuous with the surrounding bone.

Osteitis fibrosa is not likely to be so homogeneous in density, neither is it likely to be so sharply defined from the surrounding bone, or to involve only the alveolar portion of the jaw. Osteitis fibrosa is, as we shall see, usually a more diffuse involvement of the mandible.

True *osteomata* tend to arise from the body of the mandible, but it might not be possible to differentiate the two conditions radiographically.

Sarcoma might have to be considered as a differential diagnosis, but it is not likely to be so homogeneous and so dense, although it might be. The clinical features would probably suggest the innocence or otherwise of the condition.

Paget's Disease (Osteitis deformans)

A recent census of cases of osteitis deformans which have been radiographed in the X-ray departments at Guy's Hospital, shows that the condition is seen in those departments with a frequency of about one case a week. Notwithstanding this fact, I cannot recall having seen more than a few cases associated with changes in the bones of the jaws. Brailsford has recorded the fact that Paget's disease produces three different types of bony changes in the long bones, and he has described them thus :—

The *osteolithic* type in which there is uniform increase in density of the bone with obliteration of the cancellous trabeculæ so that a " ground-glass " appearance is produced (fig. 2).

The *osteoporotic* type : In this the affected bone is less dense than normal and its trabeculæ are coarser and irregularly arranged (fig. 3).

The *lithocystic* type in which there is a combination of the two preceding types (fig. 4).

These three different appearances of the condition as it may occur in the long bones are reproduced somewhat closely, but not exactly, in the jaws. Excluding the osteoporotic type, there is a resemblance between the other two and osteitis fibrosa from which it can be differentiated by the fact that in the latter condition only one portion of the jaw is involved, whereas in Paget's disease the whole of the jaw is usually affected. There is an interesting change in the appearance of the teeth which is sometimes found in Paget's disease, a more or less globular " exostosis " of some of the tooth roots. In one of the cases that I saw there were several teeth involved and the " exostosis " was even more marked (fig. 2). Such a condition of the teeth alone might lead one to investigate the long bones and skull for evidence of bony changes.

Osteitis Fibrosa

This is an interesting, if rare, condition, which has a way of appearing in unexpected places. In the well-developed cases the condition is not difficult to recognize, but in the early cases of small extent its recognition may be very difficult, or perhaps I should say it may not even be thought of. Osteitis fibrosa is the name given to different conditions ; for instance there is osteitis fibrosa cystica which is associated with parathyroid tumour or hyperplasia. In this condition there is decalcification of the bones with cyst formation and increase of calcium in the blood-serum. The jaws may be involved by cystic formation, but I have never seen a case.

There is another type of osteitis fibrosa which produces cysts in the long bones, but which is unassociated with general decalcification of the bones or with parathyroid change. The blood-serum is normal in this condition. More than one bone may be affected at the same time.

The third type is also unassociated with parathyroid or blood-serum changes. There is no general decalcification, but there is, in the affected bone or bones, a structural change, the normal bone being replaced by bone or fibrous tissue. Either of these structures may predominate, so that the radiographic appearances will depend upon which is in excess, the bone or fibrous tissue. This is the type of osteitis fibrosa that I wish to discuss.

Without wishing to attempt any classification except according to radiographic appearances, one recognizes three different " types " which are found in the jaws. There may be, however, a merging of any of the " types " in one individual.

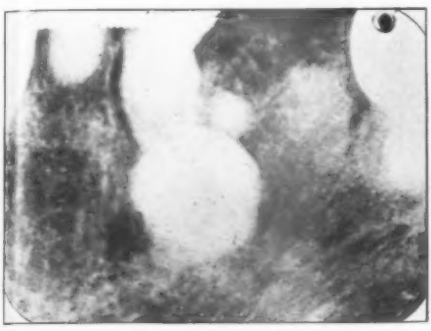


FIG. 2.—Paget's disease.

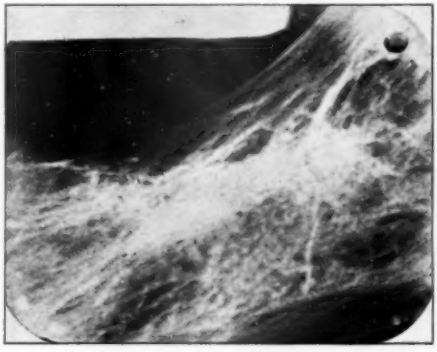


FIG. 3.—Paget's disease.

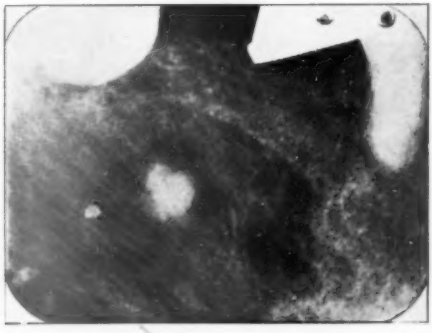


FIG. 4.—Paget's disease.

One " type " is found in the maxilla in young subjects. There is new bone formation which is relatively soft and which, on radiographic examination, resembles the outer surface of the rind of an orange (fig. 5). It may cause considerable enlargement of the affected side of the maxilla and encroach upon the antral cavity. It is sometimes said that the condition is infective, but pathologists do not agree with this.

A second " type " occurs in the maxilla in adults of any age and results in an increase in the size of the affected part, either laterally or downwards into the mouth, or both. The new bone is hard and produces a radiographic appearance which is best described as granular or simulating " ground glass ". In one case there was also a very extensive involvement of the anterior aspect of the cranium (fig. 6).

The third " type " occurs in the mandible and, in my experience, has always commenced in young subjects. The depth of the jaw may be increased considerably and the width less so, or the disease may be localized to a portion of one side of the jaw.

The radiographic appearances vary from a fairly homogeneous " ground-glass " appearance to an irregularly calcified condition with more or less dark cyst-like

FIG. 5.—Osteitis fibrosa. Type I.

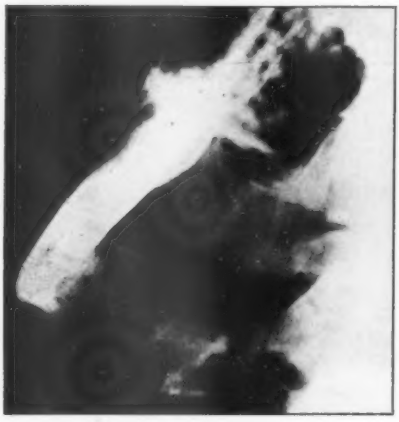


FIG. 6.—Osteitis fibrosa. Type II.

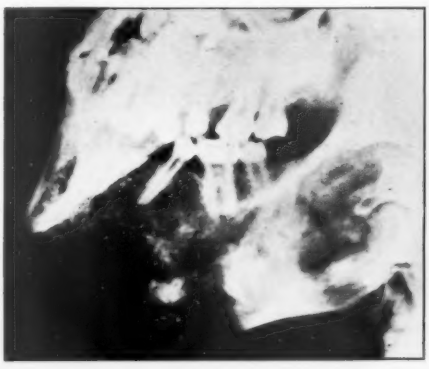


FIG. 7.—Osteitis fibrosa. Type III.

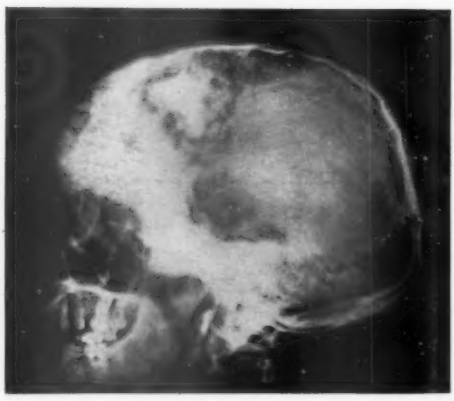


FIG. 8.—Osteitis fibrosa in skull. (Same patient as in fig. 7.)

irregular cavities in the bone (fig. 7). In all those cases that have been submitted to operation, the bone has been very hard. In one case there was extensive involvement of the anterior aspect of the cranium which was clearly not a direct extension of the disease, but a separate focus (fig. 8). I do not suggest that these three " types " are different clinical entities, but different radiographic manifestations of the same disease. So far we have only considered the extensive condition, but it is sometimes encountered in very small foci in which the possibility of osteitis fibrosa is not con-

sidered frequently enough. The localized areas vary in appearance from what looks like a condensation of bone simulating sclerosing osteitis, but lacking its homogeneous density and possibly associated with obviously new tissue formation (fig. 9) to, at the other end of the scale, obvious replacement of bone by a less dense substance, but having calcified areas in it.

FIG. 9.—Localized osteitis fibrosa.

There are types of the same condition which show any combination of the two appearances just described.

MID-LINE CYSTS (INCISIVE CANAL CYSTS)

The anterior palatine foramen or incisive fossa as it is now called, may or may not appear in a radiograph, and when it does appear it is recognized by its central position in the maxilla. It varies very considerably in size and clarity in different individuals, and may be very large without any suggestion that there is a pathological condition present. Occasionally, however, the clinical and radiographic appearance leads to the diagnosis of a pathological process in the fossa. Such a condition is usually

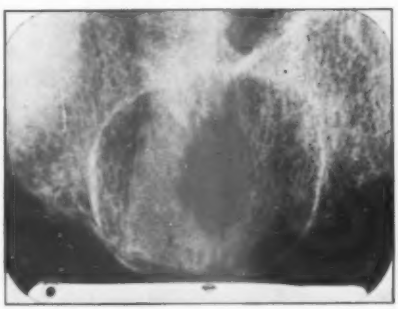


FIG. 10.—Mid-line cyst.

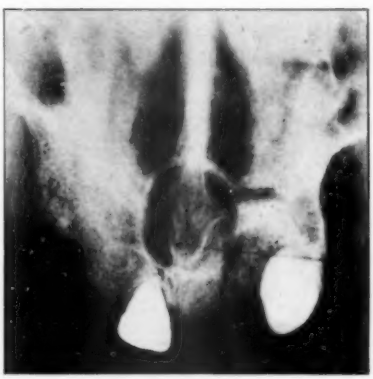


FIG. 11.—Mid-line cyst.

regarded as being a cyst, but without causal relationship with the teeth, although the disease process may spread and involve the teeth. In my experience these cysts have predominated in edentulous patients, probably on account of the fact that pressure upon the papilla in the palate by the denture has made the patient aware of an abnormality (fig. 10). Cases have been encountered which have the incisor teeth standing and, on the whole, they have offered more difficulty in diagnosis (fig. 11).

But whether dentulous or edentulous, there is revealed in the radiograph an area of bone destruction in the mid-line of the palate in the incisor region. The cavity is clearly defined by a corticated wall and varies in size considerably. The larger cysts in edentulous cases offer no difficulty in recognition, but the small ones may not be readily differentiated from a normal, but large foramen. In such a case the clinical findings would be the determining factors. In cases with teeth present, there is difficulty in differentiating the large cysts from dental cysts arising from one of the incisors. This differentiation can only be made by the recognition of persistence of normal lamina dura. A cystic cavity in the mid-line unassociated with changes in the lamina dura is almost certain to be an incisive fossa cyst. In the case of a small enlargement of the foramen in a patient with incisor teeth standing, the clinical findings would determine the diagnosis. If a radiograph shows what appears to be a large foramen, I usually consider the condition is an anatomical one in the absence of clinical evidence to the contrary. There is no appearance in the radiograph which enables the differentiation to be made, but I am always suspicious when I see a rounded " foramen " with dense cortical lining.

Epithelial Odontome (Multilocular Cyst ; Adamantinoma)

Notwithstanding that the literature suggests that this condition is common, it is considered a rarity at Guy's Hospital, where few cases of adamantinoma are seen. Most of the cases in my experience have occurred in the mandible in men, and I can only recall having seen it in the maxilla on two occasions. There are two types, the cystic and the solid, but they may occur together. The radiographic features differ in both, and as a rule it is possible to differentiate them radiographically. The cystic type is the more common of the two. The usual site is at the posterior aspect of the horizontal ramus and in the ascending ramus. The cystic type may present one of two appearances.

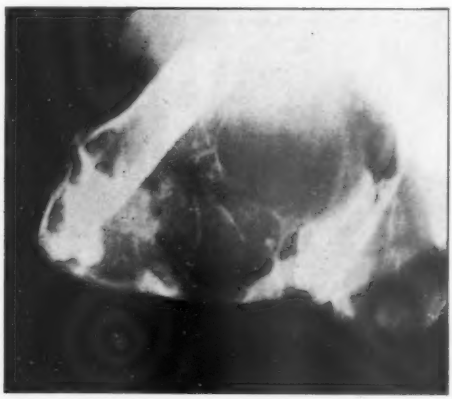


Fig. 12.—Epithelial odontome. Cystic type.

Taking the commoner type first, it is found in the ascending ramus chiefly, and extends in a greater or less extent along the horizontal ramus. From the radiographic appearances there is nothing to suggest the name of " multilocular cyst." There is a large area of bone destruction with well-defined borders, but not very clearly corticated, somewhat suggesting the presence of a large cyst which has suppurated. Indeed the only feature which permits diagnosis from a cyst is the presence of a very coarse trabeculation in the middle of the area of destruction. These coarse striæ are quite characteristic of the condition and make the diagnosis easy (fig. 12).

Another point of value is the relatively small amount of bone destruction as compared with the size of the tumour clinically.

The other cystic type is well fitted to have the name " multilocular cyst ", for it is made up of well-defined cystic cavities. The cystic spaces are large and well defined while the walls are relatively thin (fig. 13). There is sometimes an unerupted tooth in the middle of the cyst.

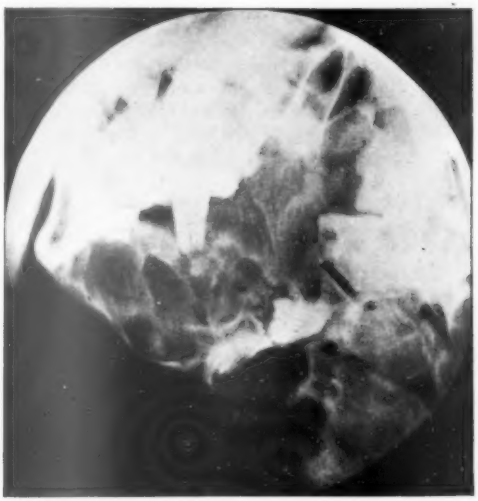


FIG. 13.—Epithelial odontome. Multilocular cystic type.

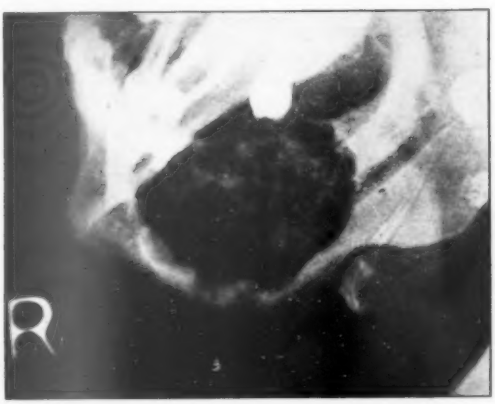


FIG. 14.—Epithelial odontome. Solid type.

The solid type of epithelial odontome shows a more or less multicystic appearance, but the spaces are smaller and the walls may be thicker. The condition is seen to resemble the previous type, but the bone spaces are smaller, less well defined, and with more bone present (fig. 14). In some cases the little spaces are well defined and

corticated, while in others the appearances suggest a honeycombed destruction of bone, so that individual holes have no clearly defined margin.

Other cases reveal the same appearance of a group of small cell-like spaces rather resembling a honeycomb. The walls of the individual cells are not very sharp, "fluffy" might describe it, but in the smaller tumours this may not be quite so apparent. In one case the radiograph revealed a combination of the cystic type posteriorly and the solid type anteriorly. It is usually possible to differentiate the cystic and solid types, but the latter is very easily mistaken for osteoclastoma. Experience of a number of radiographs shows that if the large cystic condition is present, the diagnosis can be made at once, but in the absence of the large cyst, the differentiation between the solid adamantimona and osteoclastoma may be very difficult. There may be nothing in the radiographic appearance to assist in a differential diagnosis, but it should be remembered that an adamantinoma occurs late as a rule and osteoclastoma is a condition usually found in younger people.

An epithelial odontome may become epitheliomatous, and I once obtained a radiograph of a patient in which that change had just taken place. The radiograph clearly showed the localized infiltration of the bone by the malignant change, whereas the rest of the tumour presented the typical appearance of an epithelial odontome.

Osteoclastoma (Giant-celled Bone Tumour)

This condition very closely resembles other conditions from the radiographic point of view and so it has been included for consideration. Osteoclastoma of the jaws is not by any means so frequently seen as epithelial odontome. It appears to occur in younger subjects than epithelial odontomes and, like them, has been found more often in the mandible than in the maxilla. The situation of most of my cases was anterior, but I have seen the condition in all parts of the jaws. These two points of difference between the age incidence and the sites are of some value in the differentiation of osteoclastoma from epithelial odontome. The radiographic appearances of different osteoclastomata may vary very considerably, and while a confident opinion may be given in some cases, in others it is not possible to do so. The simplest type of radiographic appearance of this condition is that in which there appears to be a cystic cavity which, instead of having a clearly defined cortical, bony lining, there is a well-marked demarcation of the cavity. The margins are not quite so definite as with a cyst and look rather as if there were abortive attempts to wall off the tumour. This is one point of distinction from a cyst, another is that there is some bony structure, perhaps very slight trabeculation only in the cavity (fig. 15). I have found this point of the greatest value in the differentiation of osteoclastoma from cyst. It is surprising how very slight the amount of trabeculation may be to enable a confident opinion to be given. The trabeculation is fine, not like that in the epithelial odontome.

Another type of radiographic appearance is one in which there is considerable expansion of the jaw with central destruction, but with more and coarser trabeculation, which is irregularly arranged (fig. 16). The walls of the expanded cavity remain bony in contra-distinction to those of a cyst of commensurate size. Furthermore, a cyst wall is usually smooth, whereas that of an osteoclastoma may be irregular; and this point has proved of value in radiographic diagnosis (fig. 17).

The third radiographic type closely resembles the solid type of epithelial odontome; indeed it may not be possible to differentiate between the two.

Points of value in the differentiation are that the osteoclastoma may show a slightly more dense cortex, and the bony walls to the cellular spaces tend to be distinct and somewhat "fluffy" in appearance. There is an impression of greater osseous reaction in the tumour with an osteoclastoma (fig. 18). It is difficult to convey an accurate description of these appearances which are clearly shown in

the radiographs. The radiologist has the radiographic features alone to guide him, and these may not be sufficient to enable a differential diagnosis to be made; with all the evidence before him the clinician, however, may be able to decide what the

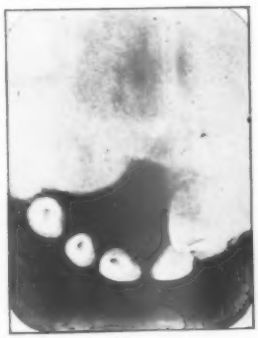


FIG. 15.—Osteoclastoma. Very fine trabeculation.

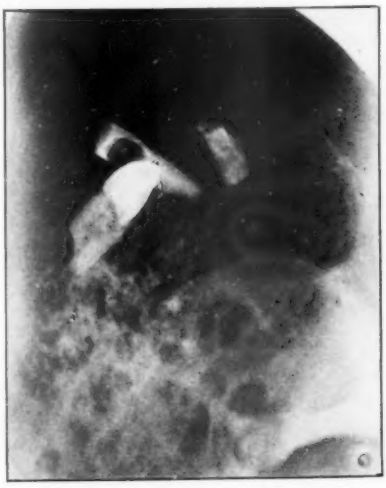


FIG. 16.—Osteoclastoma, showing bony cortex.

FIG. 17.—Osteoclastoma.

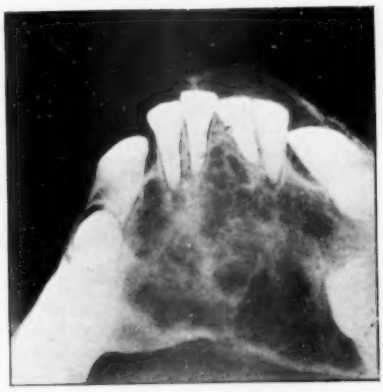


FIG. 18.—Osteoclastoma, simulating epithelial odontome.

condition really is. There will probably be a certain number of cases which can only be decided after operation and histological section. In this respect there is one case in which because the gross enlargement of the mandible was associated with

enlargement of the glands, the radiographic diagnosis was considered to be inaccurate (fig. 17). Section after biopsy produced a diagnosis of osteitis fibrosa which was obviously not correct; but on full operation, the condition was found to be osteoclastoma and further section proved it so. This experience is not very uncommon in the case of bone tumours, and it goes to show that only by a consideration of all the features, clinical, radiographic, histological, and subsequent history, can accurate diagnosis be made in doubtful cases. There have been cases in which the radiographic appearance of an osteoclastoma very closely resembled osteitis fibrosa of the focal type; and the differentiation was suggested by the fact that only a relatively small portion of the jaw was affected or by absence of typical radiographic features of either condition (fig. 18).

Neoplasms

Of the malignant neoplasms, *epithelioma* is the commonest in the jaws. It may arise anywhere in the mandible and maxilla, but it is probable that the most frequent site in the mandible is at the junction of the ascending and horizontal rami, while in the maxilla the mucous membrane of the antrum is the commonest place. The tumour does not arise in the bone but involves it by invasion, and the radiographic appearances are those of bone destruction with no evidence of any bone reaction. With the columnar or squamous-celled growths the area of bone destruction contains no bone and the edges are irregular and serrated. This irregular, serrated edge, when present, is typical of a neoplasm, not necessarily an epithelial one, but a

Fig. 19.—Carcinoma of mandible.

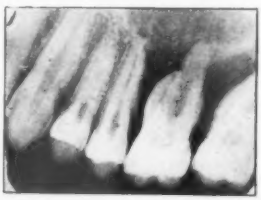


Fig. 20.—Carcinoma of alveolus arising in antrum.

malignant one of some kind (fig. 19). There is no evidence of any new bone at the edges of the growth, nor of sclerosis in the bony walls. The typical picture is that of bone destruction. In the case of the antral involvement there will be destruction of that part of the wall which is adjacent to the growth and in the affected portion of the maxilla (fig. 20).

Here again there will be no bony lining such as we may see in the case of sarcoma and which is always present with cysts and innocent growths which extend from the maxilla into the antrum. Occasionally in the case of basal-celled carcinoma a number of which have, in my experience, been seen at the posterior aspect of the

horizontal ramus, there is a saucer-shaped defect in the alveolar border, or there may be what appears to be an unhealed socket present (fig. 21). The absence of history of recent extraction and the sharply defined margins of the bony defect lead one to suspect a growth of this type, but it is not possible to be certain in the absence of histological section. One such case which I examined developed a wide destruction of mandible, notwithstanding that the tumour had been dealt with surgically and by surgical diathermy.

Sarcoma.—Is not very frequently encountered in the jaws, but it is occasionally seen. It may present a variety of different appearances as it does in any other bone, depending upon the type of growth that is present.

There is the frankly bone-destroying tumour which may not be differentiated on radiographic evidence from carcinoma ; but in complete contrast with this there is the type of growth which results in much new bone production with little, if any, bone destruction. The first is termed the osteolytic type and the latter osteogenetic, and there is a wide variation of combinations of the two processes in different tumours. As has already been intimated, the osteolytic type has similar features

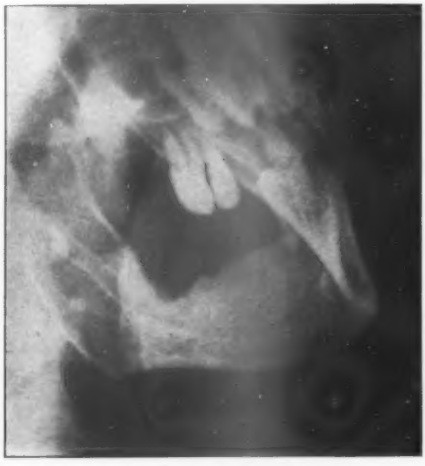


FIG. 21.—Basal-celled carcinoma in mandible.

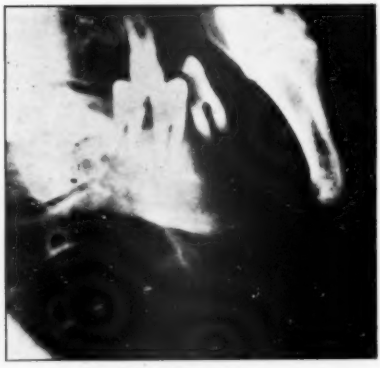


FIG. 22.—Osteolytic sarcoma.

to carcinoma and, in my experience, the only point of difference which has been of slight value in differentiating the two is that sarcoma appears to involve a wider area and greater depth of bone more quickly than does carcinoma, but this is by no means a constant finding and is not a reliable criterion (fig. 22). The edges of the bone present the irregular infiltration which is so typical of neoplastic invasion. The tumours which result in a small amount of bone reaction tend to have better-defined bony margins and may indeed be corticated. Though it resembles an osteoclastoma it may be differentiated in some cases by the sharpness of the trabeculæ in the sarcoma, as compared with the " fuzzy " outline of the trabeculæ in an osteoclastoma. These are not certain means of differentiation, but they are helpful.

In other sarcomata there is no well-defined line of demarcation of the bone, but the presence of new bone formation in the centre is of value in suggesting the probability of sarcoma. Other points of value in the recognition of a sarcomatous growth may be, that in addition to one of the former appearances, there is a definite

invasion of a normal cavity such as the antrum (fig. 23). This is a very valuable point, because the simple tumours which involve the antrum invaginate the sinus, but do not invade it. The edge of the tumour may present useful evidence: a sarcoma may be devoid of bone at its periphery (fig. 24) or there may be irregular new bone production contrasting with the smooth expansion of the bone by a cyst and the less smooth, but usually continuous, shell of the osteoclastoma.

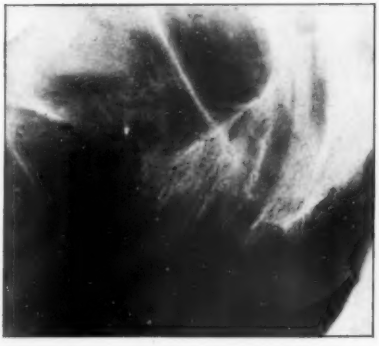


FIG. 23.—Sarcoma invading antrum.

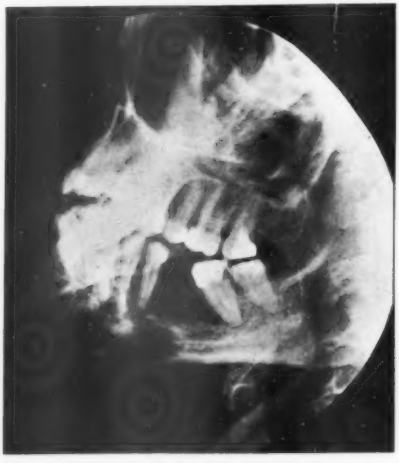


FIG. 24.—Sarcoma of mandible.

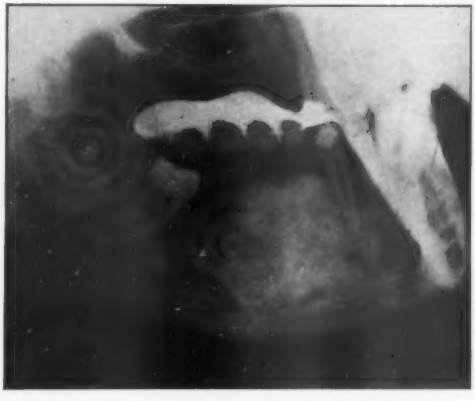


FIG. 25.—Osteogenic sarcoma of mandible.

In those sarcomata which present a large amount of new bone formation, there may be close similarity with simple hyperostosis, and only the clinical features may suggest the presence of a serious lesion. One sign which is said to be typical of osteogenetic sarcoma is the presence of vertical spicules of bone situated at more or less right angles to the bone. When present, they certainly do suggest the probability of sarcoma, but they are not absolutely pathognomonic (fig. 25). In

sarcoma, perhaps more than most bony diseases, the diagnosis can only be made by a consideration of all the evidence available and, in some cases, only by a consideration of the subsequent history. It is sometimes useful to re-examine a suspected tumour after a short lapse of time, when there may be further evidence of the greatest value. Against this it might be said that delay is not justifiable, but this would not be vital if the interval were only a few weeks.

Dr. DAVID A. IMRIE said he was very interested to hear that in many cases of osteitis fibrosa Dr. Worth found the bone to be of great density. In his experience the bone in osteitis deformans and osteitis fibrosa was soft, and in many cases the extraction of the teeth, which were often markedly exostosed, was easy. In fact it frequently happened that some portion of the bone was removed with the tooth. Assuming the correctness of the theory propounded by Lawford Knaggs that osteitis fibrosa and osteitis deformans may be due to the same condition, in individuals at different age-periods, the density of the bone encountered in young subjects suffering from osteitis fibrosa may be due to the greater activity of the osteoblastic element. In view of the comparative rarity of the osteitis deformans encountered in the dental as opposed to the general radiographic department, he suggested that Dr. Worth might examine the jaws of cases from the general department to determine whether the changes in the alveolar bone were an early or late manifestation of the disease.

The Dental Stigmata of Congenital Syphilis

By LEWIS G. CRUICKSHANK, L.R.C.P. & S., L.D.S.

Introduction.—Over eighty years have elapsed since Sir Jonathan Hutchinson, in 1857, published his original account of the dental changes associated with congenital syphilis. He stated that the upper central incisors were to be considered the " test teeth ", and that statement still holds good to-day. Congenital syphilis, like acquired syphilis, is becoming more and more a disease which in many cases can only be diagnosed by serological methods. The reason for this is either a natural mitigation of the disease, or more probably the effect of the " 914 " group in treatment. In only a very small percentage of cases does one see the classical skin and bone lesions of the textbooks.

Experience shows that there are two chief age-periods at which congenital syphilitics come under observation :—

(1) Within the first few months of birth—the period of " snuffles ", skin rashes, &c.

(2) About school age—the commonest presenting symptom being interstitial keratitis, most frequently occurring between the ages of 8 and 15, although 17–19 is a common age in females, and cases have been recorded as late as 34 (Lees, 1937).

The most diagnostic of the dental stigmata, the Hutchinsonian incisor, is present from about the 7th year onwards, and its more frequent recognition by dental surgeons might often lead to the recognition of congenital syphilis before some dramatic occurrence such as interstitial keratitis caused medical aid to be sought. The ability to recognize the clinical variants of the Hutchinsonian incisor, and a knowledge of the less common dental stigmata of congenital syphilis, are thus a matter of importance to the practising dental surgeon, the importance being from the patient's point of view rather than the dentist's, as congenital syphilitics become non-infective within a short time of birth.

Stigmata in the deciduous dentition.—Hutchinson (1887) described a condition in which " the tooth sacs suppurate, and the crowns of the teeth, almost always the upper central incisors, are exfoliated before they are cut ". This he attributed to " congestion of the gums and tooth sacs during the secondary stage of syphilis in infants ".

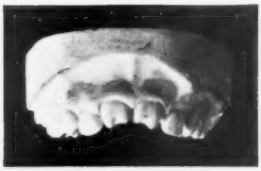


FIG. 1.—Typical Hutchinsonian incisors.

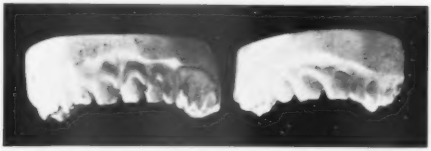


FIG. 2.—Hutchinsonian incisors. Notching not marked.

FIG. 3.—Hutchinsonian incisors. Note demarcation of three primitive denticles, with failure of development of central denticle giving rise to the characteristic wedge-shape and notching.

FIG. 4.—Hutchinsonian incisors. Notching absent and convergence of sides not marked.

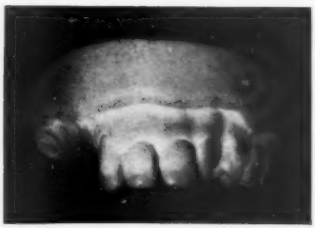


FIG. 5.—Hutchinsonian incisors. "Barrel-shaped" type. Notching absent.

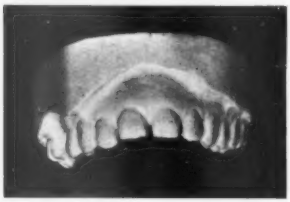


FIG. 6.—Hutchinsonian incisors. Very slight convergence of sides only.

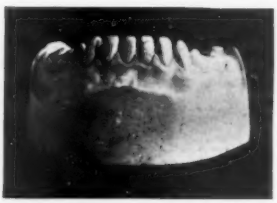


FIG. 7.—Lower central incisors of Hutchinsonian type. No notching.

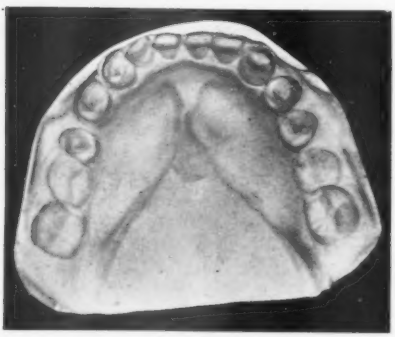


FIG. 8.—Moon's molars. Note circumferential notch on left canine.

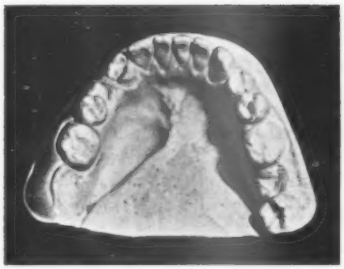


FIG. 9.—Moon's molars. Slightly less typical.

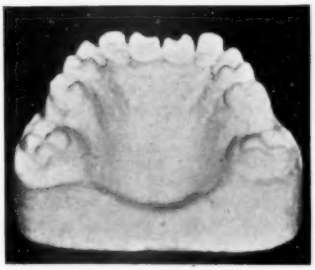


FIG. 10.—Accentuation of cingulum in lateral incisors and canines.

FIG. 11.—Severe hypoplasia, not necessarily syphilitic.

FIG. 12.—Hypoplasia of first permanent molars, simulating Moon's molars.

FIG. 13.—Open bite, associated with diminutive Hutchinsonian incisors.

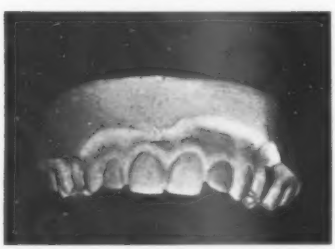


FIG. 14.—Normally formed upper central incisors. Treatment was started at the age of 1 month.

FIG. 15.—Hutchinsonian incisors (upper of fig. 7). Treatment started at the age of 3 weeks, but patient defaulted until aged 3. Insufficient treatment may thus fail to arrest the development of typical dental deformities.

He also described a peculiar form of caries in which the neck of the tooth was attacked and rapidly eaten through, the crown eventually dropping off. Other changes which have been recorded include notching of the incisors, premature eruption of the teeth, &c. Premature eruption has long been quoted as a common sign of congenital syphilis, but it is now generally agreed that retarded eruption is a more likely finding. Regarding the diagnostic value of the stigmata which he described in the temporary dentition, Hutchinson says: "They can at best rank only as suspicious, for probably states closely resembling them occur not infrequently in those who are not syphilitic". That statement applies equally to all so-called stigmata in the deciduous dentition, which in my experience are not necessarily confined to congenitally syphilitic children.

Stigmata in the permanent dentition.—(a) The upper central incisors: The classical Hutchinsonian incisor is a wedge- or barrel-shaped tooth, narrower at the incisive edge than at the gum margin. The incisive edge is typically notched in its centre, and the tooth may be diminished in size. Not infrequently there is marked spacing of the teeth, and the distal margins may be turned outwards. The deformity is generally symmetrical, but cases may occur in which only one incisor shows the typical changes. Such cases are, however, rare. There exist numerous clinical variants of the Hutchinsonian incisor which are frequently met with and must often pass unrecognized.

For purposes of classification they may be divided into two groups:—

(1) Teeth without notching of the incisive edge, but the sides of which are either parallel or show slight convergence to the cutting edge. There may or may not be diminution in the size of the tooth.

(2) Teeth without notching of the incisive edge, but with marked convergence of the sides.

The groups merge into one another, and there is wide variety within each group.

The average Hutchinsonian incisor of the former group corresponds to the "minimal Hutchinsonian tooth" described by Pitts (1927). The formation of the notch in the incisive edge is generally described as due to attrition, and the wedge-shape of the tooth as due to maldevelopment of the central portion of the tooth. Hutchinson (1887) described the presence of three or four sharp spines occupying the centre of a shallow, crescentic notch in a newly erupted central incisor. He stated that these spines would quickly break away, leaving the typical central notch. Attrition possibly contributes to notch-formation in some cases, but the demonstration of typically notched Hutchinsonian incisors by X-ray before eruption suggests that attrition is only a contributory cause (Pitts (1927), Bolam (1935)).

Observations have led me to believe that the formation of the notch and the wedge-shape of the tooth are attributable to one common process. The predilection of syphilis is for the vascular system, and the pathological process consists of an endarteritis, with later a periarteritis and characteristic inflammatory infiltration.

The mid-line of the body has, generally speaking, the poorest blood supply, and if we assume that this generalization applies to the "mid-lines" or central portions of the developing incisor teeth (themselves close to the middle line) we have grounds on which to explain the dual deformity.

Each incisor tooth develops from three primitive denticles which are in normal cases equally developed: in a recently erupted tooth these may be seen as three little tubercles on the incisive edge. If, however, the central denticle is deprived of part of its blood supply as the result of specific vascular obstruction, it may fail to calcify properly, and may also fail in growth as regards size. Failure of development in breadth results in convergence of the two lateral denticles, giving the characteristic wedge-shape. Failure of development in length results in the formation of a centrally placed notch in the incisive edge. Failure to calcify properly results in a deficient

area of enamel at the incisive edge, providing a possible additional factor in production of the notch.

The incidence of Hutchinsonian incisors is variously stated. Nabarro (1927) gives 15% and Hissard (1932) under 6%. My own figure from my series of 157 cases is 28%. Such a high incidence compared with other observers is possibly due to inclusion of atypical variants.

(*b*) *The lower central incisors :* Notching of the lower central incisor teeth is rare, but not infrequently they are barrel-shaped or wedge-shaped, corresponding to upper central incisors of the un-notched type. Changes in the lower incisors appear to be almost invariably accompanied by similar changes in the upper jaw. Diminution in size is quite a constant feature, and small peg-like teeth are sometimes seen. The incidence of changes in my series was 5%.

(*c*) *The canines :* Colyer (1923) described the deformity of syphilitic canines as a " circumferential notch near the cutting edge or point of the crown." Such a deformity does certainly exist in a small percentage of cases of congenital syphilis, but is more of interest than of diagnostic value. The presence of such a notch may give the canine, when viewed from certain angles, the appearance of a Hutchinsonian incisor. The deformity occurred in only 4·5% of my cases.

(*d*) *The molars :* The teeth affected are the first permanent molars, more particularly those in the lower jaw. The typical syphilitic molar described by Moon (1876–7) is a small, dome-shaped tooth, devoid of definite cusps, the coronal surface consisting of an irregular honeycomb pattern.

The employment of mercury in the treatment of congenital syphilis is perhaps responsible for the production of hypoplastic six-year-old molars, which are capable of simulating a true Moon's molar very closely. In hypoplastic teeth the enamel is deficient, but in true Moon's molars it is not (Hutchinson (1887)). The pathology of the deformity is explicable in a similar manner to that already given with regard to the Hutchinsonian incisor. The incidence of Moon's molars is stated by Lees (1937) to be even higher than that of Hutchinsonian incisors. In my own series the incidence was 7%, as compared with 28% for Hutchinsonian incisors.

Accentuation of cingulum in upper incisors and canines.—Hissard (1932) describes " nipple-like eminences " on the lingual surface of the upper incisors and canines, and discusses their relation with congenital syphilis. In a series of 54 cases of the disease, he found the condition in six cases, i.e. 11%. The incidence in my series of 157 cases was 10%, but as my control series of non-syphilitics is not yet complete, I am not able to make any personal observations on the diagnostic value of the condition. However, the control series to date shows a lower incidence of the condition than was found in a similar number of congenital syphilitics.

The tubercle of Carabelli.—The relationship of an antero-internal cusp on the upper first molars to congenital syphilis has given rise to much discussion. Mozer (1921) noted its presence in 40% of syphilitics and in 39% of non-syphilitics. Fernet (1928) concluded that it was suspicious only. Hissard (1932), in a series of 500 patients, found seven cases, four of which were congenital syphilitics. In a series of 54 cases of known congenital syphilis, he found 11% with accessory tubercles. Sprawson (1931) says, " A fifth antero-internal cusp is so common that the presence of this cusp or a trace of it is really commoner than the four-cusped form usually regarded as normal ". Hazen (1928) states that the supernumerary tubercle of Carabelli has been proved to have no diagnostic significance, and that view is held by the majority of syphilologists to-day.

Open bite.—The occurrence of an open bite in congenital syphilitics presents some interesting points.

Hissard (1932) describes the condition as a " lenticular space between the dental arches due to atrophy of the upper arch in height ", and states that he has never seen the condition apart from congenital syphilis. The alteration of normal bone formation

in syphilis is explicable firstly by osteochondritis in long bones, and secondly by interference with blood supply consequent on specific vascular obstruction, with fibrotic changes later. The occurrence of an open bite in congenital syphilitics would appear to be due to a combination of bony maldevelopment on either side of the mid-line, along with the frequent occurrence of diminutive teeth. There is little doubt that such a condition must exist apart from syphilis, but the combination of open bite with small and often typically deformed teeth is a striking one.

Effect of antispecific treatment.—Taking into consideration the teeth most commonly affected by congenital syphilis, and their periods of calcification, it would appear that the characteristic changes take place during the first year. *Spirochæta pallida*, the causal organism of syphilis, has been demonstrated in the dental follicle (Pasini (1908)), and its presence there brings about the vascular changes which have already been described. If antisyphilitic treatment is given regularly from shortly after birth, the characteristic dental stigmata do not develop. If treatment is not instituted until the child is 1 or 2 years old, dental stigmata may appear, as calcification of the customarily affected portions of the incisors and molars will probably be complete by then. Inadequate or grossly interrupted treatment, even if started shortly after birth, may fail to prevent the appearance of the typical dental stigmata.

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Section of Comparative Medicine

President—Thomas Dalling, M.R.C.V.S.

[*November* 23, 1938]

DISCUSSION ON THE USE OF SULPHANILAMIDE AND ALLIED DRUGS IN THE TREATMENT OF HUMAN AND ANIMAL DISEASES

Dr. L. E. H. Whitby (Bland-Sutton Institute of Pathology, Middlesex Hospital): Bacterial infections which are affected by sulphanilamide include those due to hæmolytic streptococci (Groups A, B, and C), meningococci, gonococci, *Bact. coli*, and *Proteus vulgaris*. This drug is also active against Ducrey's bacillus, *Clostridium welchii*, and Friedlander's bacillus. There is no evidence of its activity against virus infections except lymphogranuloma inguinale, or against rheumatic fever, neither is it active against pneumococci—except Type 3—nor against *Strept. viridans*. Experimentally it has some action on *Staph. aureus*.

The compounds related to sulphanilamide in which substitutions have been made in the amino group include prontosil soluble, soluseptasine, and proseptasine. The soluble preparations are useful when oral administration is impossible and when a rapid effect is required; they are quickly excreted. Proseptasine is less potent but is also less toxic, and has a useful place in medicine for mild streptococcal infections. Compounds related to sulphanilamide in which substitutions have been made in the sulphonamide group include uleron and M & B 693. Here the range of activity has been increased, especially in M & B 693, which is active against pneumococci of several types and clinically active against *Streptococcus viridans* infections. Experimentally both these compounds have some activity against staphylococci.

Both clinical judgment and common sense are necessary in order to get the best

effect with all these drugs. Additional information is required concerning optimum dosage in different infections. From animal experiments it has been shown that the blood concentration necessary for the cure of different infections is not the same. Studies of blood concentration in relation to dose have led to the formulation of clinical rules for the treatment of acute infections. This is not necessarily the optimum treatment for all infections nor is a four-hourly administration necessarily the best. With proper technique staphylococcal infections may yield more consistently to treatment. Acute generalized infections should be treated vigorously at the earliest possible moment in order to get rid of all toxæmia. If this object is not quickly attained the chance of elimination is reduced, as repeated courses have a decreasing chance of success. Chronic infections other than gonorrhœa do not readily respond to treatment with these drugs and the final elimination of the infection rests with the host. This should be borne in mind and specific therapy should not be neglected.

Dr. A. W. Stableforth (Division of Preventive Medicine, Royal Veterinary College, London): My contribution will deal with those animal diseases in which sulphanilamide or allied drugs are being tried or in which these drugs might be of value. More detailed reference will be made to the use of sulphanilamide in bovine mastitis. Dr. Whitby has stressed the fact that these drugs have proved particularly valuable in some of the acute infections of human beings. Whilst there are in animals certain acute infections, those which come under our consideration are on the whole less severe than those of human beings in whom such striking results have been obtained. These chronic infections are of such importance, e.g. the common form of bovine mastitis, that a test of the efficacy of the sulphanilamide group of drugs is fully warranted. Sulphanilamide itself has been chosen for the test in the first place on grounds of cost, as far as large animals are concerned.

Streptococcal diseases.—The streptococcal infections of animals are caused by different groups of streptococci from those usually found in human infections, e.g. Group B (*Str. agalactiae*) in the common chronic bovine mastitis; Group C in equine conditions such as strangles, pneumonia, wound infections, and endometritis, in certain cases of acute bovine mastitis and in some infections of dogs and other species; Group G in most canine and some feline infections; and certain other groups of streptococci in the more acute forms of bovine mastitis. Group A streptococci are only rarely concerned in animal disease.

There is still much preliminary work to be done in testing the efficacy of sulphanilamide or allied drugs against the various streptococci listed by *in vitro* or by mouse experiments. Last year my colleague, Mr. Hignett, and I were able to show experimentally that sulphanilamide is active against Group C streptococci, so that infections associated with this group are worthy of field experiments. There are one or two reports of successful protection of mice against Group B streptococci, but so far as I know, no evidence yet as regards Group B strains from bovine mastitis. We have tried to make strains sufficiently virulent for mouse experiments by passage, but have so far failed. There is, as yet, no evidence regarding Group G streptococci.

Bovine mastitis.—We are carrying out field experiments to find out if *Str. agalactiae* infections can be cured by the administration of sulphanilamide *per os*. The cows chosen for experiment have in all cases shown large numbers of *Str. agalactiae* in one or more quarters on at least two occasions. A cure has not been regarded as established until at least three negative samples have been obtained, the last being approximately three months after treatment began. Three variations in dosage are being tried: (*a*) 6 drachms per cwt. body-weight on three occasions at forty-eight-hour intervals, (*b*) 3 drachms per cwt. daily for five days, and (*c*) one initial dose of

6 drachms per cwt. followed by 1 drachm per cwt. every eight hours for five days. We have shown that these doses produce a concentration of sulphanilamide in the milk averaging about 10 mgm.%, although big fluctuations are found with (*a*). The work is still in progress, but it appears certain that whilst sulphanilamide given as under (*a*) and (*b*) reduces the clinical symptoms, often remarkably, it does not in most cases lead to a sterilization of the infection. This result is probably attributable to the massive invasion of the udder. Method (*c*) is still under test, but it seems that sulphanilamide is only likely to be of value in acute cases; we are trying to get further information regarding this.

The clinical experience of some practitioners seems to suggest that prontosil, sulphanilamide, or allied drugs, are of considerable value in the treatment of many diseases of horses and dogs which are associated with streptococci. Attempts are being made to get more data, particularly from the bacteriological aspect, of these infections; those in horses are often of an acute nature and in dogs are often associated with deaths in young puppies. Attempts have been made to infect puppies experimentally and then to cure them with sulphanilamide. This latter work is not yet ready for detailed comment.

Br. abortus infections.—Good results have been reported following the administration of drugs of this group in certain cases of undulant fever in man. The evidence is not yet sufficient to warrant any definite conclusion. Montgomery has reported the cure of certain experimental infections in goats, but there are, as yet, no published results regarding the use of sulphanilamide or allied drugs in bovine infections. Some work on this question is being done, but it is again too early to come to definite conclusions, although the evidence up to the present does not suggest that treatment with sulphanilamide itself is likely to prove a practical method of dealing with this infection.

In conclusion, there are two general considerations which should be borne in mind. Firstly, sulphanilamide and allied drugs are often used in suboptimal doses. Secondly, an attempt should be made to determine the exact nature of the cases treated. Progress will be hastened considerably if dosage is increased, e.g. in the case of sulphanilamide to, say, 1 grm. per 10 lb. body-weight, and if all possible bacteriological and other apposite data are obtained before and after treatment.

Dr. Claude Rimington (National Institute for Medical Research, Hampstead, N.W.3): *Disturbances of Pigment Metabolism following Administration of Drugs of the Sulphonamide Series and Simpler Related Substances.*—It is fast becoming a commonplace remark that the use of drugs of the sulphonamide series is accompanied by manifestation of toxic symptoms in a large proportion of cases. Many of these symptoms, such as dizziness and nausea, are not regarded as being serious, or of sufficient moment to warrant discontinuation of the drug. Progressive leucocytopenia or anæmia, on the other hand, denotes intoxication of a more serious character, and the utmost care must be taken to avoid untoward consequences should the administration of the drug be continued. Sulphanilamide has been recorded as having produced both hæmoglobinuria and hæmolytic anæmia in addition to a more gradual fall in the number of circulating red cells, and of the 15 recorded cases of granulocytopenia developing under sulphanilamide or prontosil treatment, nine have proved fatal (Johnston, 1938). I would particularly emphasize that the toxic effects of sulphanilamide most to be feared are those in which the erythropoietic and leucopoietic systems are involved.

In an effort to gain a clearer insight into the mechanism underlying this toxic action, an attempt has been made recently to approach the problem experimentally.

Hæmatopoiesis and the pigment metabolism of the animal are closely interrelated. During the act of hæmoglobin synthesis it would appear that there is normally formed protoporphyrin (belonging to the isomeric series III) and, as a by-product, a small quantity of coproporphyrin which, being a member of the isomeric I series, and as far as is known without function in the organism, is excreted in the urine. Urinary porphyrin excretion can thus be taken as an index of the extent of normal hæmatopoietic activity. This view, first put forward by Rimington in 1936, has received considerable support from the experimental work designed by Dobriner *et al.* (1937) and their associates, expressly to test the validity of this generalization. Disturbances of hæmatopoietic activity and function will accordingly lead to the excretion in the urine of abnormal quantities and types of porphyrin. There is no valid evidence to indicate that hæmoglobin during its normal degradation to bile pigment ever passes through a porphyrin stage, the alternative view advanced by Lemberg (1935) that oxidative opening of the porphyrin ring occurs whilst iron and protein are still in combination finding favour with most workers upon the subject. The possibility that an abnormal line of hæmoglobin breakdown might lead in certain circumstances to the production of porphyrins (Type III) is one which has been little explored, but such a possibility cannot be dismissed entirely when considering the present subject.

The toxic action of drugs of the sulphonamide series was investigated by dosing the substances orally over long periods of time to rats, maintained upon a standard synthetic diet, and determining the amount of porphyrin excreted in the urine during successive three-day intervals. Experiments with sulphanilamide, already published (Rimington and Hemmings, 1938) showed that with doses of 0·4, 1·39, and 1·5 grm. per kilo, the urinary porphyrin excretion was increased 2·5, 7, and 8 fold respectively. The fæcal porphyrin excretion was also largely increased. These porphyrins proved to be mainly coproporphyrin III together with a little of the I series isomer. When the animals were killed, the spleens were found to be much enlarged and dark in colour, and histological examination showed marked engorgement with abundant deposition of iron-staining granules and also of brownish, iron-negative amorphous pigment in the cells of the pulp. The remaining organs presented no marked abnormality. Throughout the entire course of the experiment the animals appeared well, although some loss of body-weight occurred.

In continuation of this work, other drugs of the sulphonamide series, some of the diphenylsulphones, and also simpler related substances, have been given orally to rats, and the urinary porphyrin determined as previously, in order (*a*) to find whether any relation was observable between porphyrinuric action and therapeutic efficiency or toxicity to the animal as a whole, and (*b*) to determine, if possible, what chemical grouping in the drug contributed to porphyrinuric activity.

The results are presented in the following table, in which notes have also been included upon the recorded capacity of the different substances to produce methæmoglobinæmia *in vivo*. It will be seen that within the series of drugs examined there is clearly no parallelism between porphyrinuric action and therapeutic efficiency. The toxicity of the compound, as measured by the minimal fatal dose, however, shows some correlation with its capacity to produce porphyrinuria. It is, of course, necessary to view the figures for toxicity by the mouth with some caution, as has been recently pointed out by several workers, since sparingly soluble substances such as, for example, proseptasine and disulphanilamide, do not appear to be absorbed proportionately to the dose when this exceeds a certain level. It is thus impossible to attain a blood sulphanilamide level in the mouse greater than 3 or 4 mgm.% by oral administration of disulphanilamide in any quantity (Feinstone, Bliss, Ott and Long, 1938), the maximum being attained with approximately 1 grm. per kilo.

The recognized high toxicity of 4 : 4′ diaminodiphenylsulphone was again

exemplified by the present experiments, and this substance was found to be highly porphyrinuric, whilst the corresponding diacetyl derivative, which is better tolerated, produced only a moderate increase in porphyrin excretion at a much higher dosage level.

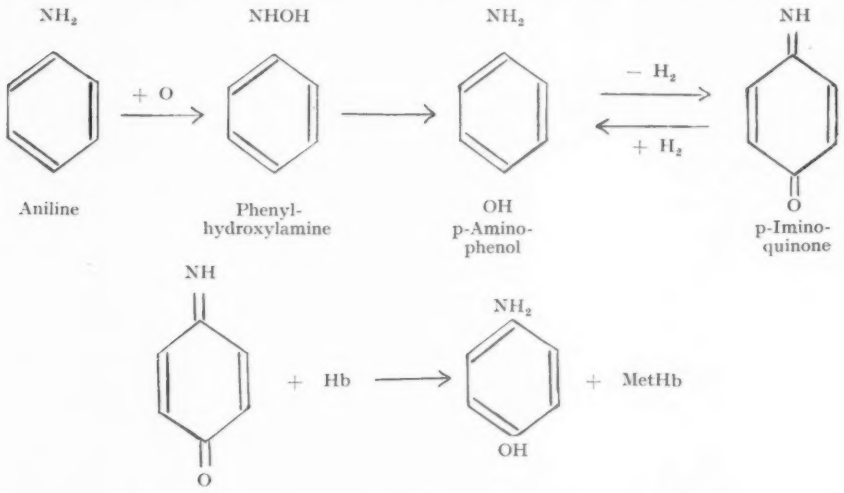
It has been concluded, as a result of experimental and clinical experience, that many of the derivatives of sulphanilamide are resolved by the body into sulphanilamide itself. My results, in general, tend to support this view. The existence of de-acetylating enzymes in tissues has been demonstrated recently by Michel, Bernheim and Bernheim (1937), who found in liver and other organs an acylase capable of removing the acetyl group from acetanilide. It is also conceivable that demethylation of substituted amines may occur *in vivo* to some extent.

Passing on from the question of general toxicity to that of the relationship between porphyrinuric action and chemical constitution, it became evident at quite an early stage of the investigation that the presence of the aromatic amino group was a factor contributing to this particular pharmacological activity. Accordingly a number of simpler amines and amino derivatives were tested by the same methods, and it was found that many of these were highly porphyrinogenic. Aniline, for example, caused a 12-fold increase in porphyrin excretion when administered at a level of 0·59 grm. per kilo, and the histological appearance of the spleen, post mortem, was strikingly similar to that following sulphanilamide poisoning. The further observation was made that of the substances tested, all those known to cause methæmoglobin formation *in vivo* were also found to cause increased excretion of urinary porphyrin. Conversely, closely related derivatives like p-phenylene-diamine, trichloraniline, and methylacetanilide, which do not form methæmoglobin, were without porphyrinuric action.

A suggestion to the effect that the responsibility for the unpleasant symptoms often following the administration of sulphanilamide is to be traced to the aromatic amino-group, has already appeared in the literature (Jennings and Southwell-Sander, 1937, following Kracke and Parker, 1933–4) and has been freely quoted, but the situation is obviously less simple than such writers infer. Not all of the toxic symptoms are related to the amino group, nor do these reactions occur after drugs such as sodium sulphanilyl-sulphanilate or disulphanilamide, in which an aromatic amino group is still present. The clue to the problem, as far as action upon pigment metabolism is concerned, is probably to be found in the observed parallelism between porphyrinuric action and capacity of the drug for methæmoglobin formation.

The mechanism of methæmoglobin formation has been most extensively studied in the case of the relatively simple substance aniline. Heubner (1913), and Heubner and Schwedtke (1936) suggest that oxidation occurs *in vivo* with the formation of p-aminophenol, probably through the intermediation of phenylhydroxylamine. Acetylphenylhydroxylamine has been isolated by Ellinger (1920) from the blood of acetanilide poisoned cats, and m-nitrophenyl-hydroxylamine by Lipschitz (1920) from the reaction mixture of minced animal tissues incubated with m-dinitrophenol. Heubner, however, does not consider the hydroxylamine to be the actual methæmoglobin former since it is irreversibly oxidized *in vivo* with ease to azoxybenzene (Heubner, Meier and Rhode, 1923), and his own studies have shown, in agreement with the work of others, that aniline introduced into the blood-stream may bring about the formation of many times its equivalent quantity of methæmoglobin; in fact it appears as if an equilibrium is established when approximately one-third of the total blood pigment has been oxidized. Aminophenol, on the other hand, is known to pass very readily and reversibly into p-iminoquinone. This could oxidize one equivalent of hæmoglobin into methæmoglobin, becoming reduced in the process, be oxidized again by the tissues, and enter into reaction with a further molecule of hæmoglobin. It would thus act as a catalyst, converting more and more of the

blood-pigment into methæmoglobin until an equilibrium was eventually established, or it itself became destroyed. The scheme is illustrated by the following diagram :—



An essential for active methæmoglobin formation, according to this theory, is, therefore, the presence of an oxidizable aromatic amino group, together, preferably, with an unoccupied p– or o– position so that a p– or o– iminoquinone derivative may be formed.

Applying these considerations to the special case in question, it will be seen that when both p– and o– positions in an amine are substituted by groups not easily removed *in vivo*—as for example in 2 : 4 : 6 trichloraniline—the capacity for methæmoglobin formation is suppressed. At the same time the ability to cause increased excretion of porphyrin disappears.

From the experimental work here presented, a fourth generalization may tentatively be suggested, as follows. The grouping effective in conferring porphyrinuric activity may be similar to that causing methæmoglobin formation, namely, an aromatic amino group, unsubstituted or potentially free, and preferably situated in such a manner that oxidation may occur, leading to a p–iminoquinone configuration.

In what manner, if at all, methæmoglobin formation and increased excretion of porphyrin are related, is still the subject of experimental inquiry. It is believed, however, that these studies may prove to be of value in assessing the severity of disturbances of pigment metabolism and of hæmatopoietic function likely to be produced by therapeutic agents, including those belonging to the class of substances under consideration.

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TABLE I.

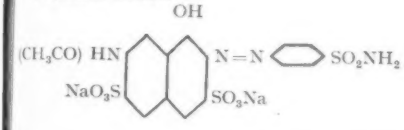
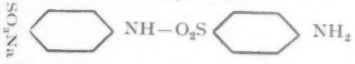
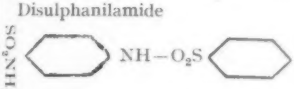
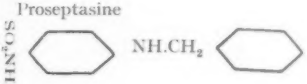
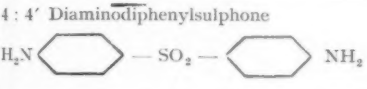
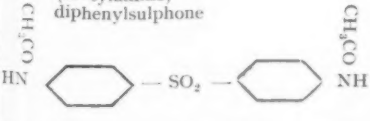
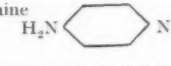
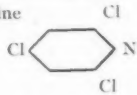
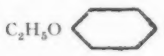
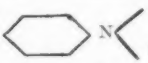
Drug	Dose conferring protection (mouse) grm./kilo	Toxicity (minimal fatal dose, mouse or rat) grm./kilo	Porphyrinuric action: Dose grm./kilo	Porphyrinuric action: Result: increase times normal	Methæmoglobin formation
Sulphanilamide 	0·25—1	4	0·4 1·39 1·5	+ 2·5 ++ 7 +++ 8	+
Prontosil soluble 	1·0	4 (intra-muscular)	1·25 2·1	+ 6 +++ 13	+
Na Sulphanilyl-sulphanilate 	Subcut. *nil* per os 2	20	0·05 0·25 1·0 (subcut.)	— — —	−
Disulphanilamide 	0·25—1	> 20	0·53 0·80	— —	−
Proseptasine 	0·5	> 20	1·0	+ 2	
4 : 4′ Diaminodiphenylsulphone 	0·0025—0·1	0·25—0·5	0·028 0·045 0·080 0·15	+ 3·5 + 3·5 ++ (Hb'uria) ++ (deaths)	+
4 : 4¹ Di-(acetylamino) diphenylsulphone 	0·25—0·1	40	0·18 0·59	++ 4 ++ 5	

TABLE II.

Drug	Porphyrinuric action: Dose gm./kilo	Porphyrinuric action: Result : increase times normal	Methæmoglobin formation
Sulphanilic acid 	1·4 1·8	– –	–
p-Aminobenzoic acid 	1·25	–	–
p-Phenylenediamine 	0·18 0·27	(+) (+)	–
Aniline 	0·35 0·59	+ 3 +++ 12	+
Monomethylaniline 	0·025 0·125	+ 3 ++ 5·5	+
Dimethylaniline 	0·054 0·26	(+) 1·6 + 1·8	+
2 : 4 : 6 Trichloraniline 	0·01 0·054 0·625	– ± (+)	–
Phenetidine 	0·044 0·22	+ 2 + 3·5	+
Methylacetanilide (Exalgin) 	0·11 0·13	– –	–
Hydroxylamine hydrochloride .. .. $NH_2OH.HCl$	0·075 0·15	++ 4·5	+
Sodium nitrite $NaNO_2$	0·18	–	+
Isoamylamine	0·11	–	–
Hæmatin	0·02 (4 mgm. i.v.)	–	

Dr. H. Loewenthal: The striking results obtained in treating bacterial infections with sulphanilamide and related drugs led at first to the neglect of immuno-therapy. Yet clinical experience and experimental work—e.g. Fleming's *in vitro* experiments with pneumococci—are now showing that even better results in the treatment of disease might be obtained when the patient's immunity is increased.

With this object in mind experiments were undertaken to find out whether combined serum and sulphanilamide treatment of streptococcal infections in mice would give better results than either method alone. Preliminary tests showed that in preventive treatment the injection of a small amount of serum resulted in the reduction of the quantity of drug which had to be given in order to secure a protective effect. Curative tests were then made, but it should be mentioned first that serum treatment alone is ineffective with hæmolytic streptococci which are pathogenic for man, when given to mice eighteen hours after infection. Sulphanilamide treatment likewise has very little effect when applied so late. In one experiment 80 mice were infected with 1 c.c. of a 10^{-7} dilution of a culture of hæmolytic streptococci and treated eighteen hours later. Of the 40 mice which received either normal or immune serum none survived, and only one out of 20 mice treated with 20 mgm. sulphanilamide survived. But 16 out of 20 mice could be saved when the drug as well as immune serum were given. The latter was prepared by the recently described method which uses young encapsulated cocci as antigen.

This result clearly suggests a synergic action of drug and serum.

Professor Alexander Fleming directed attention to the methods of testing chemotherapeutic drugs for bacterial infections. He proposed three tests:—

(1) That the chemical should, in human blood, kill or inhibit the growth of the bacteria in a concentration which it was possible to attain in the body by the therapeutic use of the drug. Also in this concentration it should not interfere with the activity of the leucocytes.

(2) When injected intravenously into an animal it should confer on that animal's blood an increased antibacterial, bactericidal or bacteriostatic power. This increase would be at its maximum immediately after administration of the chemical if the action was a direct one, but if the drug had to be changed in the body into some active substance then the maximum increase would only be manifest later.

(3) The clinical test by which it is ascertained whether the chemical, when administered to infected animals, can cure the infection.

He stressed the importance of the *in vitro* tests and showed that by these great differences could be detected in the sensitivity of different streptococci and pneumococci to drugs like M & B 693. As the action of M & B 693 was purely bacteriostatic the actual killing of the bacteria had to be done by the body, and it therefore followed that the greater the immunity the greater would be the apparent effect of the chemical. When the infecting microbe was very sensitive to the drug, as was the case with *Streptococcus pyogenes* and some pneumococci, the drug was likely to be successful without any increased immunity, but where the microbe is less sensitive, as with some pneumococci and gonococci, then much better results should be obtained by the combination of chemotherapy with immunotherapy, either active or passive.

This synergic action of chemotherapy and immunotherapy has been shown clinically in gonococcus infections and in streptococcus infections of animals.

Mr. L. E. W. Bevan felt that his recent practical experience in Southern Rhodesia lent support to some of the views expressed by previous speakers. In 1921 he had drawn attention to the association between contagious abortion of cattle in Rhodesia

and undulant fever of man. His observation that one was communicable to the other, was met with some scepticism, but had since been proved to be correct. His daughter, a little girl of 5½ years, in August 1937, when recovering from measles, contracted Brucella infection by drinking unboiled milk from a dairy where subsequently 26 out of 40 cows had been proved to be suffering from abortion disease. Dr. Stableforth had told them that there was evidence that the sulphanilamides exerted some effect upon *Brucella abortus* infection of animals, and he could assure them from his personal experience that certain of them did exert a specific effect upon *Brucella abortus* infection of man. He had watched his own case for over nine months, having treated her and recorded the reactions following the administration of proseptasine and sulphonamide–P. In the absence of exact knowledge of the appropriate and safe dose, he could only administer infinitesimal quantities, but had immediately found that proseptasine did exert a specific effect, ameliorating the symptoms and reducing the temperature. The reduction in temperature was not as dramatic as in the charts exhibited by Dr. Whitby ; on the contrary there was at first some elevation in the evening temperatures for some days, followed by a gradual decline for perhaps eight days before normal was recorded. Unfortunately cure was not effected by these small doses ; after longer or shorter intervals relapses always occurred. These relapses were sudden and prolonged and required a course of small doses of proseptasine before they were shut off. After two months of such treatment cure was despaired of, and fouadin, which at that time was much vaunted as a remedy for *Br. melitensis* infection, was tried. When a course of increasing doses from 1·5 c.c. to 5 c.c., a total of 22 c.c. in all, had been given intramuscularly, the child was so dangerously ill that the treatment had to be discontinued. Shortly after, Dr. Isadore Rosin, with whom he had discussed the effects of proseptasine, kindly advised him that he had obtained a complete cure of a little girl of 11 who had contracted the disease after measles and at the same time and from the same source as the speaker's daughter, by using massive doses of sulphonamide–P. A serious relapse compelled him to risk this treatment with doses as large as could be supported with safety. Again the symptoms disappeared and the child improved rapidly ; but again the thermal decline was gradual and after an interval relapse occurred. This was immediately arrested with a further exhibition of the drug in large quantities. Finally, after the third relapse had been noted at the onset and shut off by sulphonamide, the child appeared to recover. For seven months no further relapse had been observed ; this experience had convinced him that small and inadequate doses did not cure but brought about a subacute infection with relapses which might become acute. He believed it was only by applying massive doses within the limits of safety, capable of sterilizing the patient of the brucellæ, that cure—and perhaps immunity—could be obtained. This would not be an economic proposition in the treatment of bovines. He agreed with previous speakers that it was most necessary to obtain an early and correct diagnosis, and to apply the drug when infection was acute, if the best results were to be obtained. In this view he was strengthened by his experiences in the treatment of *Tr. rhodesiense* infection with Bayer 205 or antrypol. If subcurative doses were administered relapses, and finally death, followed. But if massive doses were given the animal was not only sterilized of the parasite and cured, but acquired immunity against reinfection. In the latter cases the electric charge of the plasma of the recovered animal was reversed and the adhesion phenomenon occurred. He believed that in electrophoresis might be found the explanation of some of the mysteries associated with the sulphanilamide and allied preparations which had been discussed that evening.

Section of Ophthalmology

President—Malcolm Hepburn, F.R.C.S.

[*November* 11, 1938]

The Abiotrophies of the Retina and Choroid

By Arnold Sorsby, F.R.C.S.

Abstract.—(1) Hereditary lesions fall into three groups:—

(*a*) Malformations: Present at birth.

(*b*) Abiotrophies: At birth the tissue is fully differentiated but it undergoes degenerative changes at some period in post-natal life.

(*c*) Phakomatoses: A group possessing features of the two previous groups and some features of neoplasms.

(2) The conception of abiotrophy draws attention to a large group of affections which have a hereditary character and develop in apparently normal tissues, making their appearance in different families at different periods of life. The conception is well established in neurology. Ophthalmology offers numerous examples. A large variety of familial fundus lesions (other than hereditary congenital anomalies), the corneal dystrophies (generally setting in at about puberty), "senile" cataract (occurring with regular frequency in certain families at certain ages), all illustrate the occurrence of familial groups of affections in tissues that show no obvious congenital anomaly, structurally or functionally. Whether this group is called heredo-degenerations or abiotrophies or by some other name is of little significance in comparison with the recognition of the existence of such a clinically distinct group.

(3) The understanding of the nature of these affections is rudimentary. Studies in the mode of inheritance of the different abiotrophies help to explain their distribution, but not their nature, just as the genetics of congenital malformations do not explain the embryological mechanism underlying these defects.

(4) The earlier workers of this branch of genetics were inclined to attribute the degenerative process in post-natal life to a failure inherent in the cell. Present evidence indicates that in the abiotrophies it is the environment of the cells rather than the cells themselves that is at fault. Work along these lines has already led to valuable therapeutic results in affections that were previously regarded as incurable (acholuric familial jaundice; Schüller-Christian syndrome).

(5) The abiotrophies of the retina and choroid are indicated. The solution of the problems they present lies in the study of their general associations. These are discussed.

(1) Retinal Abiotrophies

(i) *Generalized retinal lesions.*—Typical retinitis pigmentosa (primary retinal type); choroidal form of retinitis pigmentosa; retinitis pigmentosa sine pigmento; retinitis punctata albescens and its relationship to fundus albipunctatus; choroideremia, total, partial, and spurious; gyrate atrophy, garland type, multiple colobomatous type, and disseminated pigmentary type.

(ii) *Central retinal lesions.* The macular dystrophies (degenerative, hæmorrhagic, and exudative types).

(iii) *The central and paracentral lesions.* Doyne's choroiditis; angioid streaks; the C. family.

(2) Choroidal Abiotrophies

(i) General choroidal sclerosis.
(ii) Central choroidal sclerosis.
(iii) Peripapillary sclerosis.
(iv) Central and paracentral sclerosis.

(3) Retinal Abiotrophies with Recognized General Associations

(i) The lipoidoses.
(ii) Demyelinating affections.
(iii) The hereditary ataxias.
(iv) Elastosis dystrophica.
(v) Other affections.

Illustrative Cases

Retinitis Pigmentosa Sine Pigmento

I.—Mrs. M. S., aged 33.

Vision with correction $\frac{6}{12}$, both eyes. Fields down to fixation point. Night-blindness. Discs and arteries characteristic of retinitis pigmentosa. A few specks of pigment are present.

II.—Miss R. H., aged 18.

Vision with correction: R. $\frac{6}{12}$, L. $\frac{1}{60}$. Night-blindness. Fields down to fixation point. A few specks of pigment are present.

III.—C. L., aged 68.

Vision with correction: R. counts fingers; L. $\frac{6}{12}$. Fields down to fixation point. Night-blindness, discs and arteries characteristic of retinitis pigmentosa. The absence of any marked pigment changes and the presence of the characteristic post-cortical opacities seen in retinitis pigmentosa is a striking feature.

Retinitis Pigmentosa. Mixed Pigmentary and Punctata Albescens Type

Miss P. S., aged 31.

Vision with correction $\frac{6}{6}$, partly. Family history clear. Note: (1) Remains of punctata albescens best seen downwards and upwards in left eye; (2) the typical pigment corpuscles. These have increased in number during the past three years; (3) generalized whitish sheen.

Familial Central Choroidal Sclerosis

G. R., aged 66.

Vision: Counts fingers at 1 m., both eyes. Fields full. The fundus appearances are of the type described by Nettleship as senile areolar choroidal atrophy.

The patient's brother is likewise affected.

Trouble began at the age of 20.

(Previously demonstrated: January 1935, *Proc. Roy. Soc. Med.*, **28**, 527, Sect. Ophthal., 35.)

Terminal Stage of Generalized Choroidal Sclerosis simulating Partial Choroideremia

W. A. C., aged 45.

Vision with glasses: R. $\frac{6}{24}$, L. $\frac{6}{6}$. Progressive trouble began at about the age of 20. Considerable choroidal sclerosis and atrophy. An older brother is similarly affected. Patient's sister, aged 53, has vision of R. $\frac{6}{6}$, L. $\frac{6}{9}$ (with correction). Her fundi show a small central lesion.

Partial Choroideremia

S. S., aged 27.

Vision defective since childhood. Not getting worse. Vision with correction: R. $\frac{6}{24}$, L. $\frac{6}{60}$. The choroidal circulation is present in a rudimentary fashion; there is no sclerosis.

Family history.—Negative.

Two Familial Cases of Central and Peripapillary Choroidal Sclerosis

Miss G. C., aged 60, and Miss E. C., aged 61.

These patients were demonstrated before the Section in December 1936 (*Proceedings*, **30**, 386, Sect. Ophthal., 32).

The interest in this group is the onset late in life (at about 50).

Central Choroidal Sclerosis (non-familial)

Mrs. W. W., aged 65.

Sight failing for about fifteen years. General condition satisfactory (blood-pressure 160/110).

Discussion.—Mr. FREDERICK RIDLEY showed the pedigree of a family he had observed. In one generation there were two females who both died early, actually at 44 and 39, before reaching the age at which the lesion made its appearance. But presumably both might have developed the condition, because both had daughters who either had the condition or, while not themselves having it, transmitted it to their descendants. The condition was a choroidal abiotrophy which came on at about the age of 44 and showed a dominant inheritance. It illustrated the magnitude of the problem they had to consider.

He showed a picture of the fundus of the affected daughter of one of the women with this condition which was just commencing. It was probably a choroidal degeneration with diffuse fine, pigmentary disturbance in the retinal layers. He showed also a picture of a sister of the same patient at a later stage of the condition. She showed a central area of degeneration, around which was an area of hard white exudate looking rather like retinitis circinata, and further out there were points of choroidal degenerative change. In a following picture he showed the final stage of the condition in a man now aged 53, a typical central choroidal sclerosis.

This was evidently a dominant abiotrophy affecting both males and females at about 44 years of age, involving the second eye within two or three years, central vision being lost within six years. The pictures he had shown were very dissimilar, and yet they must represent the course which this lesion took in the family whose pedigree he had brought forward. Of one of the cases he had taken the case records, which showed that in 1931 the right vision was $\frac{6}{12}$ with pigmentary changes in the right macular region. The left vision was $\frac{6}{9}$, and hyaloid bodies in the macular region were noted. Six months later the right vision was the same as before, but hyaloid bodies in the right macula were noted. In 1932 the right vision had dropped to $\frac{6}{18}$, and included in the case records was a sketch showing in fair detail the choroidal atrophy, retinal pigment, and hæmorrhage. The right eye in 1936 counted fingers only, and presented a picture they had already seen. Evidently, therefore, this particular case had been through all the stages illustrated, starting with a fine widespread disturbance of retinal pigment.

At various times—this was an important point—these appearances had been described as hyaloid bodies, pigmentary retinal degeneration, choroidal atrophy, retinal and choroidal exudate

and hæmorrhage, and degenerative changes at the posterior pole following a blow on the eye. The treatment had included the elimination of septic foci, the Wassermann reaction, and very full general investigation.

The condition was undoubtedly an abiotrophy, meaning an inherited restriction of the expectation of life of a particular tissue, in this case affecting the choroid. The diversity of the appearances seen was striking. Nevertheless, the similarity of age incidence and clinical course, in the three cases brought forward, and the fact that a dominant form of inheritance was shown stamped it, he said, as a definite clinical entity.

The PRESIDENT (Mr. Malcolm Hepburn) said that there was a great deal which might be brought forward on this subject, but there was not time to discuss it at any length. In the first place, he thought they had gone very far outside the original meaning of the word "abiotrophy" as he understood it. It was applied in the first instance to a primary degeneration exactly as Mr. Ridley had just described it, and was originally used to explain certain diseases of the nervous system, an epiblastic structure. But now it has been extended to explain many diseases of the choroid, a mesoblastic structure. Again what did the author mean by the environment of the cell? Did he mean the tissue fluids in which the cell was situated and through which it was nourished? If so, many of these conditions were not abiotrophies at all, but secondary degenerations. Further, the author had said that nobody had claimed that as much as two-thirds of the choroidal circulation was affected in pigmentary degeneration of the retina. He (the speaker), on the contrary, affirmed that not only two-thirds but practically the whole of the posterior ciliary circulation was affected, though not to the extent of completely cutting off the blood supply.

There was much more he would like to say on the subject, but time forbade.

Mr. ARNOLD SORSBY (in reply) said that the brief discussion had been of extreme interest in emphasizing how little was known of the early stages of choroidal sclerosis. When they spoke of choroidal sclerosis they had in mind something different from their conception of retinal sclerosis. The earlier stages of choroidal sclerosis were difficult to make out simply because the choroidal circulation was masked. If they were ever to understand the earlier stages of choroidal sclerosis it would not be by direct inspection of the choroidal vessels but by examining the finer disturbances in the fundus, as seen in the two first cases Mr. Ridley had illustrated.

With regard to what the President had said concerning abiotrophy, any vital conception changed with time. A tribute was due to the early workers in the field who were arrested by the fact that these tissues died early in life. That, after all, was the basis of this particular group of conditions. So far as was known, the tissue was normal up to a certain point in life and then died. Whether it died from inherent lack of vitality of the cell or because the environment of the cell was no longer suitable for life, was a minor point at the present stage. The important thing was to recognize that here was a large hereditary group which did not fall into the category of hereditary malformations. Surely it was well not to continue the argument whether the cell itself or the environment of the cell was at fault, but to go on looking into the metabolism of these particular cells or into the general metabolism in the endeavour to find the pieces of this puzzle.

Two Cases of Spring Catarrh treated by Radon.—A. D. GRIFFITH, F.R.C.S.

I.—E. S. A., male, aged 27. Railway clerk.

Eyes inflamed for a month in April 1935. The condition recurred in April 1936, and persisted. Left eye worse.

The left upper lid was given five applications of radon at intervals of about three months, from May 22, 1937, to March 19, 1938. At the first treatment the duration was twenty minutes; at all others it was thirty minutes. The right upper lid was given only one treatment of thirty minutes, on October 30, 1937.

Radon seeds containing 40 millicuries were applied in a curved, hollow applicator, of which the anterior wall, next the lid, was of silver, 0·2 mm. thick, and the posterior wall, next the eye, was of platinum, 1 mm. thick. The effect of this was to subject the palpebral conjunctiva to practically unscreened radon, whereas practically all the

β particles were screened from the eye. Before inserting the applicator the posterior surface was smeared with Müller's ointment (wax and paraffin) to absorb some of the secondary β particles. In fact, the treatment caused no conjunctival reaction.

Treatment of a non-malignant condition like spring catarrh with radiation is a completely different problem from treatment of new growths. There is no question of using the selective action of radiation on young, actively growing cells. One depends on the secondary action of radium; that of stimulating fibrosis and causing angiosclerosis. Treatment must, therefore, be long, and one cannot expect improvement until time has elapsed for the appearance of these changes, which are well shown in the anæmia of the tarsus in the cases shown.

II.—Peggy L., aged 13.

Spring catarrh, affecting both upper lids—duration when first seen, three years.

In this case only the left eye, the worse, has been treated. The same applicator was used as in the last case, with the same strength (40 mc.) of radon, but the time was one hour on each occasion. Three applications were made at intervals of about three months. The side treated is cured, and shows an anæmic tarsus; the side which has not been treated is rather worse.

I propose to treat the right side with low-voltage X-rays, and compare the results. One cannot draw conclusions from a comparison of two cases, but I note that the case which received the greater dose of irradiation was cured more quickly.

Sarcoma of Ethmoid, treated by Intra-orbital Radon.—A. D. GRIFFITH, F.R.C.S.

W. J. M., male, aged 28, was seen by Mr. James Healy, of Llanelly, in October 1937, with a small, soft swelling below and mesial to the left eye. There was slight proptosis. Mr. Healy removed a piece of the tumour for microscopy, the report on which was "fibrosarcoma of low malignancy".

The patient was sent to Westminster Hospital, where he was admitted under the care of Mr. Stanford Cade on December 2, 1937.

I saw him the next day, and found a small, soft swelling at the lower and inner part of the left orbit. There was no proptosis. Slight restriction of abduction of the eye. The corrected visual acuity was R.V. $\frac{6}{6}$ and L.V. $\frac{6}{18}$. Fundi normal.

X-ray examination by Dr. Peter Kerley showed a tumour eroding the floor of the orbit and the inner wall of the maxillary antrum. Some of the ethmoidal cells had been destroyed, but the tumour did not extend right through the posterior ethmoid cells.

A course of treatment with hard X-rays was given: twelve daily exposures of ten minutes each.

On January 11, 1938, I inserted into the orbit, through a conjunctival incision, with Souttar's seed-gun, 18 radon seeds, each containing 0·75 mc., with screenage 0·5 mm. platinum. They were distributed along the lower part of the inner wall of the orbit as far back as the optic foramen. At the end of the operation there was so much proptosis that the lids were stitched together.

There was a good deal of conjunctival reaction, but this subsided in a week and the lids sutures were removed.

A piece of tumour removed at the operation was examined by Dr. R. J. V. Pulvertaft, who reported that it was a fibrosarcoma of low degree of malignancy.

In July 1938 there was no sign of tumour. There was no proptosis, the lens was clear, and the fundus was normal. The corrected visual acuity had improved from $\frac{6}{18}$ to $\frac{6}{9}$. A new development was a sector-shaped, interstitial opacity in the cornea below, due, I imagine, to damage to a ciliary nerve behind the globe.

"Facial Hemiatrophy" with Eye Complications.—H. BAKER, M.R.C.P. (introduced by Mr. ARNOLD SORSBY).

Maud S., aged 33.

History.—Right-sided atrophy of face, neck, tongue, ears and breast, for eighteen years. Small areas of atrophy right arm. During 1923–25 had three fat transplantation operations, but the transplanted fat atrophied. Inability to close right eye completely for three years. Right tarsorrhaphy for recurrent corneal ulcer, 1936. Epiphora, and poor vision right eye, one year.

On examination.—Striking asymmetry of face: atrophy involves all tissues from skin to bone, including cartilages of ear, nose and tarsal plates. Right ear much smaller than left ear. Infantile right breast. Atrophy of skin and fat of right side of neck. Hemiatrophy tongue and palate. Patches of old sclerodermia right arm. Atrophied muscles retain good power and normal electrical reactions except right frontalis. Scar involves nerve supply to frontalis. Right eye: Enophthalmos; full movements; cannot be completely closed by lids; dilated pupil, with no reaction to light and variable reaction on accommodation. Corneal opacities present. Left eye normal.

Commentary.—The majority of cases of facial hemiatrophy show pupillary anomalies, probably of sympathetic origin. Other eye complications are extremely rare.

This case illustrates several interesting points in a rare disease. One, is the presence of pupillary anomalies; many cases of facial hemiatrophy show such anomalies. Secondly, the patient has had severe corneal ulceration, and there have been few such cases recorded in literature. Few cases out of the 450 described have shown such extreme atrophy of the tissues, and this is the fourth case recorded in which atrophy of the cartilage of the ear has occurred. In addition to the ear, this woman shows atrophy of the cartilages of the nose, and the atrophy has spread down the neck and has involved the right breast, which is infantile.

The fact that she has some areas of sclerodermia in the right arm is of importance in the discussion of the pathogenesis of this condition. Both diseases may have a common pathology, in view of their frequent association in the same patient. In many other conditions such as syringomyelia and in any disease involving the brain-stem, we see occasionally sympathetic involvement, and there are a number of these cases which have developed facial hemiatrophy. Here the eye changes suggest a lesion involving the sympathetic nervous system.

The patient has undergone three fat-transplantation operations, with only temporary improvement. It is reasonable to assume that if the fat transplantation had been done after the disease had burnt itself out, the fat might have persisted longer. There is only one muscle paralysed, namely, the frontalis, because the fat transplantation operations involved an incision cutting across the branch of the facial nerve going to the frontalis. Apart from this, the muscle function is very well preserved in spite of the severe atrophy.

Flint has described a case of facial hemiatrophy with similar eye changes of corneal ulceration, pupillary anomalies, and enophthalmos.

Stief reported a case with keratitis and cataracts.

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Mr. L. H. SAVIN said that he had one of these cases. It was not so advanced as the one shown by Dr. Baker, but the face was considerably atrophied, especially around the right side of the mandible. There were no pupillary or ocular changes. At one time this patient had phthisis, and it was remarkable that the only three cases of progressive facial hemiatrophy which had come to autopsy had all had pulmonary tuberculosis in one form or another. The suggestion was made in a recent article that the pulmonary tuberculosis caused the facial hemiatrophy by affecting the sympathetic at the pleural apex. He did not know whether that was so or not in his own case.

He had been interested to notice in Dr. Baker's case the association with sclerodermia. His own case had not got sclerodermia, but in two of the cases which went to autopsy the report stated that there was a peripheral lesion of the 5th cranial nerve from the Gasserian ganglion downwards. In view of the association of sclerodermia in so many cases, and particularly in the one shown that evening, he did not see how the theory of an uncomplicated 5th nerve lesion could possibly hold water. There were a large number of cases in which Horner's syndrome was reported as an associated condition, and this pointed to the fact that in a certain number the sympathetic must be affected, though it was a matter for further investigation whether the involvement was in the course of the 5th cranial nerve or not.

A Light Threshold Apparatus

By RANSOM PICKARD, C.B., M.S.

THE object in designing this instrument is to conform to the standard suggested by the writer in the Ophthalmological Society's *Transactions* (56, 1936, 219–229) that the testing area should subtend a solid angle of 1° at 1 metre, and that the position of the stimulated portion of the retina should be accurately defined.

The apparatus consists of a box of vertical section 6 in. square, its antero-posterior axis being 5 in. It is divided into two compartments, the posterior 1½ in., the anterior 3½ in. antero-posteriorly. In the posterior is a piece of "pot opal" glass, 2 in. square, illuminated by two lateral 6-volt lamps. The opal glass gives a reflected light of 25 foot candles.

The anterior chamber has four revolving discs, mounted on an antero-posterior spindle. These have circular apertures, six in that nearest the examinee, five in each of the others. In these apertures are Wratten neutral filters, of the strengths shown in the table.

1st disc ..	0	0·01	0·005	0·001	0·0005	0·0001
2nd disc ..	0·75	0·5	0·25	0·1	0·01	
3rd disc ..	0	0·75	0·5	0·25	0·1	
4th disc ..	0	0·75	0·5	0·25	0·1	

In the lower half of the anterior face of the apparatus is a hole subtending 1° at 1 metre. By a spring device the holes in the discs can be brought behind and in a line with the hole in the anterior face. In the septum between the two chambers is a hole in alignment with the hole in the anterior face and with the centre of the opal glass in the posterior chamber.

To ensure that, under ordinary testing conditions, the fixation point is tested, there are two round spots of luminous paint, half an inch in diameter, on the anterior face of the apparatus, on a level with the test aperture, and each 2 in. from it, one on either side.

If the source of the electricity is the main supply, a transformer must be interposed.

Method of use.—The discs are put in the position of greatest transmission, viz. 0, 0·75, 0, and 0. The front disc is rotated till the densest filter through which the light is perceived is found and left in that position. The next disc is similarly rotated and fixed, and so on for the remaining two discs.

The light threshold equals the light value of the opal glass (25 foot candles) × transmission of the first disc × transmission of second disc × transmission of third disc × transmission of fourth disc.

The examinee must have the tested eye on a level with and opposite to the light aperture. The head rest of a slit lamp does excellently for this purpose. Instructions are given that the light to be observed is midway between the two spots of luminous paint and on the same level.

The progress of dark adaptation can be observed during its course, should this be desirable. Should it be wished to investigate the field, the lamp remains fixed and the luminous spots are covered. An iron bar bent to the form of a quarter of a circle of 1 metre radius has on it a small movable plate, on which is a circular spot of luminous paint half an inch in diameter. This is moved outward and fixed by the examinee's eye. The lamp thus tests the field on the opposite meridian, and by varying the light filters the light threshold of any spot may be ascertained. To be comparable with the threshold of the fixation point, the sighting disc must be stationary. A convenient method if the whole field is to be examined is to find the threshold for a spot in one meridian, and explore the other meridia, with the same light value, thus getting an isopter for that value.

Convergence Rule

By C. G. Schurr, F.R.C.S.Ed.

There were two objects in view in designing the convergence rule. The first was to produce an instrument which would forge a link between consulting room and orthoptic department, by means of comparable readings. And the second was to try to differentiate between convergence insufficiency due to cerebral fatigue (retina occipital cortex-fusion centre), and that due to neuromuscular inadequacy (fusion centre—3rd nucleus—internal recti). This differentiation is necessary because fatigue cases require treatment such as vitamin A and rest, as opposed to orthoptic exercises.

To attain the former, the instrument had to be graduated from the mid-point of the line joining the centres of rotation of the eyeballs, and the scale had to be readily convertible into angular deviations. To procure the latter, it seemed necessary to make the " fusion pull " as strong as possible. This can be achieved by making the dissociation of the two eyes as little apparent as possible to the patient, by means of the principle of the anaglyph. He will then maintain fusion to the limit of his muscular co-ordination.

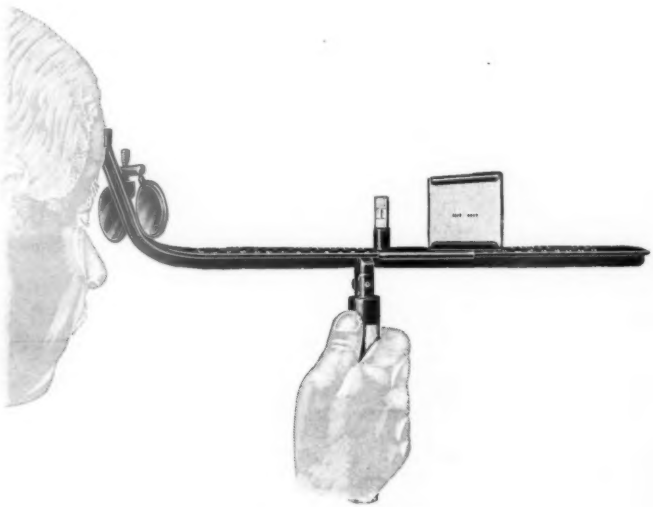
The convergence rule is held by the patient, with the head-piece pressed firmly against the glabella. The graduations on the rule are in centimetres. And a reversible slide holds the test cards, and also a small piece of glass etched with a vertical vernier line.

The vernier is used with the white card, and is an adaptation, with his permission, of Livingston's subjective test on the binocular gauge. The readings on the rule are about 1·5 cm. greater, owing to the different zero point.

The vernier line will appear in the centre between the red and green dots on the white card, if the patient is using both eyes equally. If it appears to be towards a red dot the right eye is fixing (*master eye*). Conversely, if towards a green dot, the left eye is fixing.

For the anaglyph tests, the holder with red and green complementary glasses is slipped into the socket on the descending portion of the rule, and the tinted cards are used, with the slide reversed. For all these tests, the red glass should be in front of the right eye, and the slide should be placed at 33 cm. to commence with.

When the card with the ball on a stick is in the carrier, a patient who has *simultaneous perception* will see both objects. The ball may sway slightly with the normal involuntary eye movements. If the ball appears to be off the stick, the patient has no fusion at reading distance. There is exophoria if the ball is to the right of the stick, and esophoria if it is to the left.



Convergence rule

(*Block kindly lent by Messrs. Rayner and Keeler*)

Move the slide steadily along the rule towards the patient until he says that the ball has come off the stick, and then stop. The scale reading should be taken. If the ball returns to the stick, at that point convergence is becoming unstable, a fact of some importance. When the ball remains off the stick, the point has been reached where convergence breaks down altogether, i.e. the *near point of convergence*.

A printed scale is supplied with each instrument showing the angular deviation, for a P.D. of 30 mm., of each eye for a given distance on the rule. The corresponding angular deviation multiplied by 2 will be approximately the reading in degrees of the near point of fusion on the synoptophore. Vice versa, synoptophore readings can be converted into linear distances in centimetres by referring to the scale.

If the patient says, at any distance, that the ball or the stick has disappeared, the fact that there is *suppression* of the left or right eye respectively is disclosed.

The card with the square, ball, and diamond, is a test for *stereoscopic vision*. When the red glass is in front of the right eye, the right-hand object (square) stands forward. As the objects are not related to each other, the test is difficult. And the patient may not discover the right answer for a few moments.

Discussion.—Dr. F. C. B. GITTINGS said that the instrument did not appear to give a proper convergence. On the synoptophore he himself converged about 20° and the normal was about 40°, but with this instrument, although he knew his power of convergence was below normal, he could converge up to 9 cm., which was a very considerable amount. He thought there must be some "snag" in the instrument.

Mr. SCHURR said that he had tried this instrument in one form or another for a year, and he thought the only "snag" about it was that the pull was strong, but it was made strong intentionally. A large number of patients did give exactly the same readings as with the other instrument. He had tested it several times.

Section of Epidemiology and State Medicine

President—J. A. H. Brincker, M.B.

[*October* 28, 1938]

Convalescent Hospitals of the Future: Their Type, Function, and Use

PRESIDENT'S ADDRESS

By J. A. H. Brincker, M.B., D.P.H.

I

Factors in Planning and Designing a Convalescent Hospital

A convalescent hospital not only needs special planning and designing but, in its planning and designing, those natural advantages of the site which we look upon as health-giving should be utilized to the fullest extent.

I propose now to deal with the more important of these natural advantages under their respective headings, more especially as they affect Littlehampton and its suitability as a site for the convalescent hospital the London County Council is about to erect for children; and among these advantages I intend to refer in greater detail to sunshine and radiation, for these I hold to be amongst our most valuable allies in the promotion of health and the curing of disease.

The effectiveness of a convalescent hospital depends on the suitability of its situation as well as upon its design, equipment, and staffing; and the suitability of the situation depends very largely on climatic and local conditions and on how advantage is taken of these to meet the various needs of the patients.

The conditions usually described as climatic and local include:—

(1) Site, i.e. nature of the surrounding country, character of soil, drainage facilities, availability of public services, proximity to the sea.
(2) Temperature of the air and prevalence of snow and frost.
(3) Rainfall and humidity and prevalence of mist and fog.
(4) Wind.
(5) Sunlight.
(6) Temperature of sea water and facilities for sea bathing in the case of seaside resorts, and
(7) Character of the natural water and the provision made for the treatment of various diseases, in the case of spas.

Site.—The ideal site for a convalescent hospital is one which is situated in the open, well away from streets and houses and trees, so that it may benefit to the fullest extent from sunlight and freely circulating air. It should have rising ground on the north, north-east, and south-west, to protect the buildings from the winds coming from these quarters. The site should slope gently to the south, the soil should be dry and warm, and the subsoil preferably rocky or chalky. Clay, owing to its capacity for retaining water, makes the soil wet and the air damp and cold, and is unsuitable.

It should be provided with efficient drainage and have available water, gas, and electric supplies. Moreover, it should be readily accessible to the population it serves.

The site at Littlehampton, to which reference has already been made, which is situated within the Worthing Rural District, satisfies these conditions; it faces south, slopes towards the sea, has the South Downs to the north, is protected on the south-west by the promontory of Selsey, and the subsoil is porous, consisting of gravel on chalk. It gets the sun most of the day. There is good drainage and water, electric and gas supplies are available. The water is obtained from the Worthing Corporation Supply at Patching. The sewage system, completed in 1934, serves the parishes of Angmering, Rustington, East Preston, and Kingston, and discharges through disposal works at Kingston into the sea; it works satisfactorily. The site is easily reached by train and road from London.

Temperature of the air.—The tonic quality of the air of a seaside resort depends on many factors. Chief amongst them is the temperature of the air, which should oscillate slowly between maximum and minimum; this oscillation is due to air currents from both the land and the sea and these, in their turn, are influenced by the nature of the soil, by neighbouring hills, by the power and amount of the sunshine, and by the humidity of the air.

As we are dealing with persons who require the maximum of open-air life with suitable exercise, and who should spend even their sleeping hours in the open air, the air temperature most suitable for a convalescent hospital would be a moderately tonic one, similar to that enjoyed in the Harrogate and Buxton Spas for nine months of the year.

The following table gives the temperatures for 1937 and the average temperatures for fifteen years at Littlehampton :—

Month	Temperature 1937		Temperature Average for 15 years	
	Maximum	Minimum	Maximum	Minimum
January	47·6	38·7	45·81	36·60
February	49·0	39·6	45·44	37·07
March	46·2	35·4	48·95	37·59
April	55·4	44·2	52·81	40·88
May	60·7	48·9	59·85	46·43
June	66·1	51·7	64·55	51·35
July	67·6	55·8	67·83	55·57
August	70·7	55·9	67·90	55·32
September	64·6	51·0	64·69	51·87
October	60·0	47·6	58·03	46·72
November	50·0	37·8	50·51	40·23
December	44·2	34·8	45·92	37·11
Total	682·1	541·4	672·29	536·74
Average ..	56·84	45·11	56·02	44·73

This table shows that, as regards temperature, Littlehampton may be classified as a resort with a moderately tonic climate, the minimum in winter seldom reaching the freezing point. From the records kept snow would appear to be rare in Littlehampton, and no heavy falls have been experienced for a number of years. On an average during the past ten years, snow fell on approximately three occasions a year. Similarly, night frosts are infrequent. In 1937 the temperature fell just below 32° F. on 38 occasions.

Rainfall and humidity.—Rainfall affects climate in various ways, increasing the humidity of the air, reducing the amount of sunshine, making the ground wet, and so militating against the enjoyment of an open-air life with walking and other exercise.

A humid climate has a tendency to make everything—bedding, furniture, walls, &c.—damp during the colder months and to be close, depressing, and soporific in

summer. On the other hand a very dry climate in winter tends, owing to evaporation, to chill the skin and predispose to relapse or to a state of inability to enjoy open-air life.

The average humidity at Littlehampton varies from 71% in June to 89% in December. The occurrence of mist and haze depends upon the barometric conditions prevailing in the Channel, but when they occur they are usually experienced in the early morning and disappear with the sun.

A table giving particulars of rainfall at Littlehampton is as follows :—

Month	Rainfall		No. of days on which rain was recorded
	1937	Average for 28 years	
January	5·53	2·94	25
February	4·96	2·12	24
March	4·02	1·74	19
April	2·37	2·15	16
May	2·25	1·85	14
June	1·18	1·64	9
July	1·42	1·99	10
August	1·57	2·15	4
September ..	2·03	2·37	14
October	2·43	2·78	11
November	1·99	3·13	10
December ..	3·76	3·28	20
Total ..	33·51	28·14	176
Average ..	—	—	Average for past 15 years 176

The following further table gives the rainfall in Littlehampton and in certain other seaside resorts, showing how suitable Littlehampton is for a convalescent hospital such as it is proposed to erect there :—

	Littlehampton	Eastbourne	Margate	Falmouth
Rainfall : Total amount (in inches)	33·51	38·16	30·16	43·28
Average for six winter months (for last ten years (in inches)	30·34	31·53	21·14	35·15

Wind.—Although there should be a good circulation of air on the site, convalescent hospitals should not be exposed to strong and cold winds and gales. In this country, during certain months of the year, north and north-east winds prevail and these are not conducive to open-air life on the part of people who are not robust. At other times south-west winds, which frequently attain gale force, are experienced, and these also are to be avoided.

The prevailing winds at Littlehampton are from the south-west to north-west. As the site is not in an exposed position gales are rare, and the few experienced have been from the south-west.

Sunlight.—Of all the sources of energy at our disposal sunlight—solar radiation—is by far the most important. It is essential for our very existence.

We read in the Book of Genesis that, after the heavens and the earth were created, God said " Let there be light ", and there was light. The Ancient Egyptians looked upon the sun as their god. Aristotle included light in his four elements—earth, air, water, and fire (that is light and heat). Man is a creature of sunlight, and his growth and progress are associated with sunlight. Radiation, therefore, whether it be the natural radiation of sunlight or artificial radiation, has tremendous importance biologically and physiologically, and indeed psychologically, for brightness and colour influence our mental life. Contrariwise, absence or want of sunlight breeds anæmia, disease, and ultimately death.

But one may have too much of it as of other good things. Excessive radiation may result in sunstroke and paralysis of the central nervous system. When the human being is exposed to it in excess, over a long period of time, he develops nervous exhaustion, and this leads to degeneration of the physique generally. Modern views attribute this to over-ergosterolization of the lipoid tissue and thus to over-stimulation of the body.

Intensity and duration of sunlight are therefore important factors in human evolution.

Light is usually accompanied by heat and, therefore, when considering the effects of exposure to light on the human individual except in such places as the high Alps its heating effects must not be forgotten.

It has been said that a man working in the open is exposed to a thousand times more sunlight than a man who does his work indoors. This is important for us who live in towns and do all our work indoors. All town dwellers must therefore suffer more or less from radiation starvation. In the process of evolution man has again proved his adaptability as regards his power to make up for radiation deficiency and to ward off excessive radiation. This wide adaptability to radiation is due to the human skin.

Solar radiation on the surface of the globe is an environmental factor and varies within very wide limits, being dependent upon season, latitude, contours of the earth's surface, height, humidity, presence of trees, &c., and, indirectly, on the presence of large stretches of land or water and on currents whether in the atmosphere or in the sea.

Sunlight and radiation are important in promoting health. Radiation, whether it consists of rays of long wave-length such as are used in diathermy, of short waves (infra-red), of the rays of the visible spectrum, or of near ultra-violet rays, has its useful part to play in the life of man. The human skin, through its complex capillary blood and nervous systems, regulates the amount of blood, and so of hæmoglobin, on the surface exposed to radiation.

The surface displayed by the red blood-cells covers an area of about 30,000 square feet, or nearly two-thirds of an acre, and the hæmoglobin in these cells absorbs completely the nearer ultra-violet rays, some of the shorter infra-red rays, and selected rays in the visible spectrum. It is clear that the blood is a machine of immense possibilities; capable of storing up and delivering energy and so playing a very important part in our body metabolism.

In fact radiation, through the blood, is closely associated with the development and functioning of the various vitamins, and directly or indirectly the latter govern the processes of digestion, absorption, and assimilation of food. It is essential in metabolism and growth, and it controls the inflow into the system of calcium, phosphorus, and iron.

Absence of suitable and sufficient radiation may lead to disease, such as rickets, anæmia, &c. In others, although it cannot be said that absence of radiation produces the disease, we know that artificial radiation assists in its cure—as for instance in myxœdema and in various conditions of osteoporosis, &c.

"The Biologist in Search of Material" records a series of cases where the conditions of devitalization observed, which amounted to hypotonia in women and deficiency of iron in men, were not cured either by improved feeding or by drugs but improved rapidly after exposure to sunlight, especially where this was associated with exercise and sleep.

Winter, when solar radiation is at its minimum, is the time when droplet infections are most prevalent. It is the season for respiratory diseases of all kinds, for septic infections, and for deficiency diseases. Solar or artificial radiation, therefore, is necessary not only to maintain health, but also to enable the human mechanism to function at its highest efficiency.

The value of artificial radiation is recognized for instance in keeping miners and night-workers in good health, and in the training of professional footballers and boxers.

This effect of sunlight upon the human economy was appreciated long ago. For instance, in one of the sacred books of the Hindus the recovery from old age is ascribed to sunlight: "A study of life admonishes us to revere the lamp of the heavens, the sun; and to repose in its gorgeous glow the unreserved confidence that its light shall illuminate the labyrinthine passage of unknown life and lead the curious mind to the treasure chest of unfathomable secrets."

The following table shows the amount of sunshine Littlehampton enjoyed during 1937 and over a period of twenty-three years:—

Month	Sunshine		No. of days on which sunshine was recorded
	1937	Average for 23 years	
January	63·7	64·11	17
February	71·2	85·76	20
March	128·3	142·48	26
April	144·7	165·08	26
May	195·8	224·16	27
June	257·3	235·07	30
July	154·4	224·04	30
August	236·1	214·13	31
September ..	184·2	168·32	29
October	113·8	125·79	28
November	96·1	75·53	23
December ..	47·6	57·27	17
Total ..	1693·2	1781·74	304
Average	daily 4·64	daily 4·88	Average for past 15 years 303

The following further table gives the sunshine in Littlehampton and in certain other seaside resorts and shows how suitable the locality is, from this point of view, for a convalescent hospital:—

Sunshine—	Littlehampton	Eastbourne	Margate	Falmouth
Total hours	1693·2	1690·2	1553·3	1579·5
Daily average hours	4·64	4·63	4·26	4·33

An adequately equipped light treatment department will be provided, in the proposed new convalescent hospital there, to supplement solar radiation.

Temperature of sea water and facilities for sea bathing.—The temperature of sea water has a dominating influence on the climatic conditions of a seaside resort. Water, owing to its high specific heat, is capable of warming the surrounding air without itself undergoing much loss of temperature. For the same reason water takes a long time to become heated to a temperature congenial for bathing. The temperature of sea water is important in the case of children convalescing from various illnesses. They must not be allowed to paddle until the temperature has reached at least 58° F., and complete immersion in sea water must not be permitted until the temperature is at least 60° F., and even then the time of immersion must be strictly regulated by the reaction of the individual child.

The optimum temperature is usually between 65° and 68° F. The selected and acclimatized child is first allowed to paddle for a short time which is gradually extended; later, the body is sprayed with sea water; and finally, but only after some days, if the patient reacts satisfactorily, total immersion is permitted. On leaving the sea the child should always experience a feeling of well-being, warmth, and exhilaration. The length of time the child is allowed to remain in the water depends entirely on the reaction which follows immersion, but the time may be gradually extended in almost all cases. The best time for bathing is about two to three hours

after breakfast, and if there is then a rising tide and the day is bright and sunny, the best results may be anticipated.

The temperature of sea water in the English Channel is coldest during February and March and highest in July and August. It is more quickly heated, however, in land-locked estuaries like Chichester Bay and Hayling Island, where it usually reaches 60° F. in early June and remains above 60° F. until late in October.

At Littlehampton, which is more open to the sea than Hayling, bathing may generally be indulged in from about the middle of June until the middle of October.

The Millfield site is on the sea and has its own beach of about 250 yards—sandy with some pebbles—directly accessible from the hospital grounds. There is an additional 200 yards of beach which can be made available, if required.

The effects on children of a stay at the seaside and of sea bathing are so well and clearly expressed by Sir Henry Gauvain in his writings that I am tempted to quote him in full. He says : " As the health of the child improves, as his power of response increases, sun and air bathing, supplemented by sea bathing, may be recommended with confidence. For the healthy and vigorous all these may be commenced with advantage as soon as the coast is reached. For the less robust, or those recovering from illness but otherwise of good physique and constitution, it is desirable to get acclimatized for a few days before commencing any form of bathing. The weakly cachectic, freckled, marasmic child, the child with the muddy complexion and lethargic in habit, who does not bronze readily on exposure to sunlight, with little response to natural stimuli, rarely does well. Very few sick children under the age of 5 years derive real benefit ; for them the less vigorous and clamant conditions prevailing inland are to be preferred. The stimulus of sun, open air, tonic sea breezes, and still more stimulating sea bathing, makes too heavy a call on their vitality ; they have not adequate powers of response." . . . " Marine treatment offers a ready means of influencing basal metabolism ; controlled loss of heat from the body following exposure to cold air or water necessitates the generation of heat in the body. Work has to be done. More food must be consumed, digested, absorbed and built up in the tissues. Further oxygenation is called for and there is greater elimination of waste products through the lungs, kidneys, skin and bowels. This heightened tissue change takes place not only in healthy but also in diseased tissues ; hence the process of repair in the latter is intensified and expedited. Under the influence of sun, air and sea water, muscles long atrophied fill out and become firm and hard, the patient enjoys a sense of physical well-being and an important aid to cure has been accomplished."

Spas : Character of natural waters and provision for treatment of various diseases.—Spa treatment, as an effective curative measure, is of long standing, and has an honoured history. It is not, as most people imagine, a monopoly of continental health resorts. On the contrary there are many British spas, and they have been responsible for much of the progress made and scientific research carried out in the treatment of hydrotherapy. One of the oldest spas is our own Bath, much frequented by, and highly popular amongst, the aristocracy of Roman Britain, by whom it was known as " Aquae Calidae," or " The Warm Waters," or " Aquae Solis " or " The Waters of the Sun ", just as Buxton was known as " Aquae " or " The Waters ". Researches carried out at our British spas have led to many discoveries and remedies for disease, and in hydrotherapy we have a potent agent by means of which many chronic diseases, such as rheumatism, liver, heart and digestive disorders, and paralytic conditions, can be ameliorated, if not cured.

In all spas the essential factor is the physical characteristic of the natural water, but treatment depends for its success on how this water is used and in what way it is applied to the sufferer, internally and externally. At the same time accessory processes such as massage after or during immersion, associated with diathermy, electric treatment, ultra-violet treatment, &c., are used. These aids are necessary

and now well understood; in certain conditions of ill-health, such as toxæmias, degenerative changes, morbid deposits, or disturbed innervations, the effect of the waters is different from what it is in health, and such accessory processes are essential. According to the disease, therefore, a tonic or sedative spa treatment is advised.

Similarly, seaside resorts have their special characters and favourite methods of treatment. At the same time the value, in connexion with such treatment, of occupation, interest, amusement, and exercise, is now appreciated, and these adjuncts are carefully studied and catered for. Every spa and seaside resort has its public gardens, bands, amusement halls, solaria, and bathing establishments. These all help in producing the condition of well-being in the individual and are powerful agents assisting in his cure. We all appreciate and recognize conditions around us as cheerful or gloomy, cold or warm, restful or exciting, &c., and they produce a corresponding effect. Similarly, certain occupations may have an energizing, tranquillizing, or subduing effect upon our minds, and they may be more than ever necessary when we are ill.

Education and Occupation

The importance of education and occupation in promoting the health and efficiency alike of the nation and of the individual is generally recognized. It is an axiom that to keep well and efficient, it is necessary to be occupied. The Registrar-General has pointed out that, of all males between 21 and 65, the mortality of those without occupation is twice that of those with occupation.

It is now also accepted that education and occupation are equally essential in the treatment and cure of the sick. The interaction of mind and body in health and disease is fully recognized, and it is well known that anxiety neuroses, especially if superimposed upon physical disease, often prove the greatest obstacles in the cure of the sick, more particularly if the patients are children. In these cases the best remedy is the appropriate form of physical or mental occupation.

One has only to consider the condition of those children suffering from orthopædic diseases who, of necessity, have to lie continuously in abnormal and restrained positions for many months on end. How necessary it is to prevent their introspective brooding on their sad lot, from creating mental complexes, producing anxiety and resentment, which in their turn react harmfully upon their physical state and so retard the process of reparation and cure! Moreover, children who spend long periods in hospital without education naturally become retarded in comparison with their fellows. They not only lose the education they would have received if they had not been in hospital, but also much of what they may have acquired before they were taken ill and admitted to hospital.

Education and occupation, in the form of graduated exercises, games, or walks, as well as education in its more restricted sense, whether that be formal or informal, are recognized methods of treatment, especially if they are provided as far as possible in the open.

These should be provided under medical advice and only in proportion as the patient may profit thereby, bearing in mind that children in convalescent hospitals are there because they are below par and that their physical and mental faculties are easily fatigued.

Hospital schools, therefore, are an essential part of treatment in all children's hospitals, more especially in those where children are kept for any length of time and where they are up and about. Where children are being treated in hospitals in which educational facilities do not exist it is important that they should be transferred, as soon as possible, to establishments where they can be suitably educated and occupied. In such institutions not only are skilled doctors and nurses needed, but also teachers who have been trained in the needs and requirements of the physically subnormal child.

Education and occupation, therefore, as they affect sick children, should be considered from two points of view :—

(1) They should be a means of preventing retardation as far as education is concerned.

(2) They should be regarded as therapeutic agents, promoting and hastening cure and giving the child a brighter and healthier outlook.

The type of education generally advised for sick children in hospital is the *individual system* as opposed to the *class system*. The advantage of the former is that the child is left free to progress at its own individual rate ; there is no educational pressure, and no need to classify children according to age and educational attainments.

II

I have now dealt with the general *desiderata* for convalescent treatment and the extent to which it is hoped to provide them in the convalescent hospital for children which the London County Council is about to erect at Rustington, Littlehampton.

Description of Rustington Convalescent Hospital

A short description of this hospital, as it is hoped it will appear when completed, may be of interest.

The site at Rustington (fig. 1 A and B) consists of two parts. On one [A] there stands the existing Millfield Convalescent Hospital, erected by the late Metropolitan Asylums Board on a site which covers about 8 acres and has a sea frontage of 750 ft. The shore is protected by a sea wall and a number of groynes which have prevented erosion by throwing up a bed of shingle 50 ft. deep. The shore itself is made up first of shingle for about 50–100 ft., and then of sand and shingle mixed, the distance between high-water and low-water marks being 550 ft. Thus there exists a satisfactory shelving beach suitable for bathing and paddling. The existing establishment was opened in 1904 as a convalescent home and consists of four buildings, one of which is used as administrative quarters and the other three for accommodating 98 children. The other part of the site [B] is the property called Seafield Court, adjoining Millfield. It covers 7 acres, with a sea frontage of 600 ft. It has a small residence standing on it. It is proposed to combine these two sites [A and B] and provide a composite convalescent hospital for about 500 children which will incorporate the 98 existing beds.

The hospital will provide beds for :—

(1) Orthopædic cases transferred from hospitals in London which require change of air in circumstances in which the orthopædic condition may continue to be treated. It is anticipated that a month or two's sojourn at the seaside will improve their power of recovery ; the patients will then naturally be returned to the parent hospital.

(2) Selected cases of rheumatism which it may be considered will benefit by a stay at the seaside.

(3) Pulmonary cases, such as bronchiectasis, asthma, &c., which do not do well in London.

(4) Cases convalescent after serious operations, e.g. appendicectomy, or after severe illnesses, e.g. bronchitis, pneumonia.

(5) And 352 beds for a variety of other types of disease which need open-air treatment by the sea in order to aid in their cure.

The patients' accommodation will consist of pavilions and wards constructed on open-air lines, each holding either 80 children who do not require active medical and nursing attention (figs. 1B and 2) or 20 to 30 children who do require more detailed nursing ; 20 to 30 being the number of such children a sister can be expected to take charge of (fig. 1A).

These wards are designed so that in suitable weather they can be made to open, in their entirety, on the south aspect, and in less favourable weather closed either in part, or completely, a sufficiency of through ventilation being,

however, always provided. Although the convalescent wards (fig. 2) hold as many as 88 beds these are all subdivided into groups of four by glass partitions reaching to a height of 6 ft., so that the risk of cross-infection during sleeping hours and even with the windows closed in inclement weather, is reduced to a minimum. This risk, moreover, is further diminished by the arrangement of the beds parallel, and not as usual at right angles, to the walls. The wards (fig. 1A) open on to

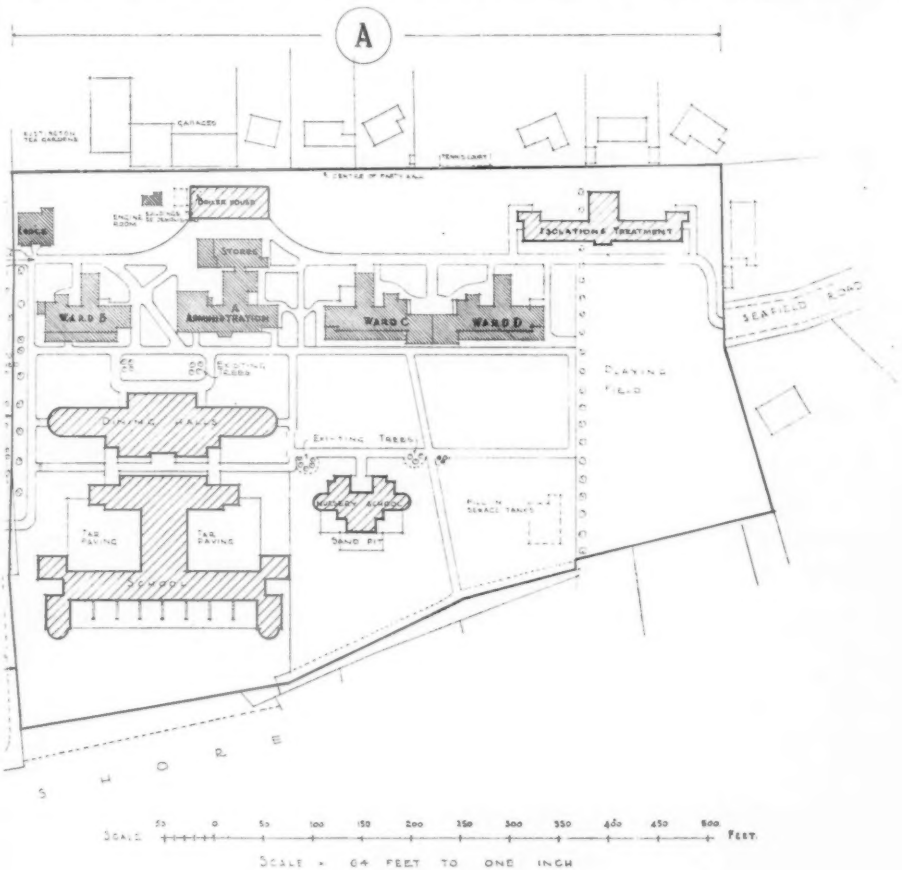


FIG. 1A.

platforms on the ground floor and on to balconies on the upper floors so that, in sunny weather, the beds and cots may be taken out and the children exposed to solar radiation, as may be considered advisable. On the north side the windows will be adequate for lighting and ventilation, and the communicating doors will be on this side leading to the bathrooms, lavatories, storeroom, ward kitchen, &c.

There will be a special treatment block (figs. 1A and 3) containing an operating theatre for minor and, in emergencies, other operations; major operations

will normally be reserved for performance at the parent hospital in London. There will be a completely equipped X-ray department, a light treatment department—which will be necessary to supplement solar radiation during the winter months when such radiation is deficient—a massage department, a plaster and dressing room, and other accessories.

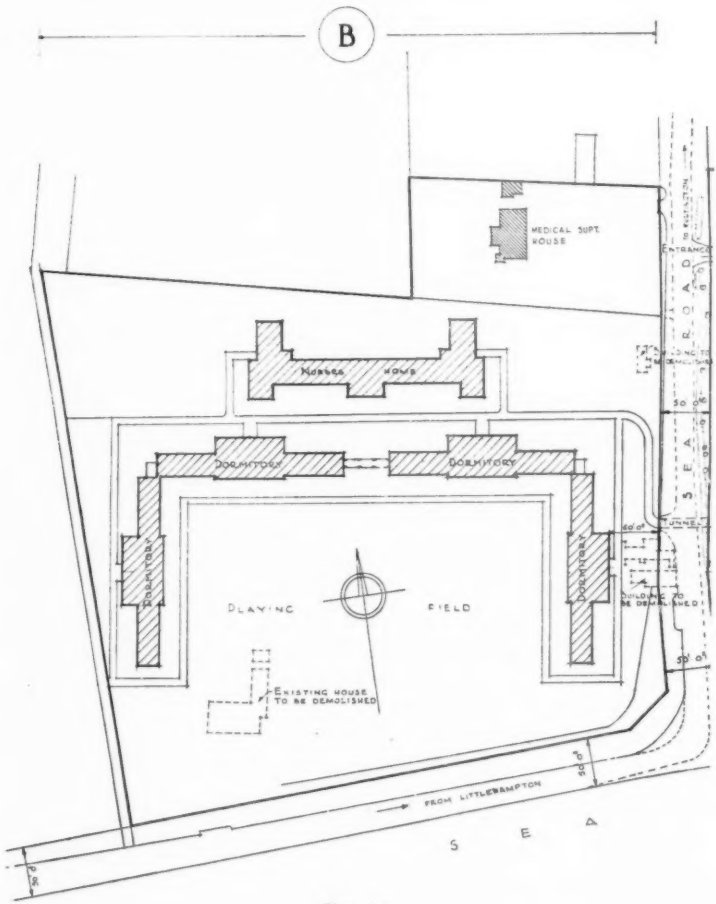


FIG. 1B.

There will also be a laboratory (fig. 3) equipped to carry out research in matters affecting metabolism and nutrition on which there is much to be learnt, and such incidental work as may be required in connexion with the diagnosis of infectious conditions. In this laboratory it is hoped that an attempt will be made to determine the effect of ultra-violet light on the recovery of cases of anæmia, and on the repair of fractures, and to ascertain whether radiation has any influence on the body's metabolic processes that is to say to carry out a detailed study of the mechanism of calcium,

phosphorus, and iron metabolism. If, for instance, it can be shown that radiation, coupled with other seaside conditions, accelerates the healing of fractures, we shall have made a great advance in dealing with children suffering from a variety of orthopædic ailments.

It is well established that, even when all preventive measures are adopted, there still remains a risk of infectious diseases occurring where children of various ages and from different institutions and homes congregate. It is essential, therefore, to provide an isolation department in all children's hospitals, where children who are sickening for, or are suspected to be suffering from, an infectious disease may at once be transferred. This block at Littlehampton (figs. 1A and 3) will contain 14 completely isolated independent wardlets or chambers, open on the south side and joined by a corridor on the north side ; attached to this pavilion will be a kitchenette, a sister's observation room, bathroom, sluice room, &c.

In addition there will be a central kitchen (figs. 1A and 4) where all the food for patients and staff can be prepared, and a common dining room where the children who are up and attending school can be fed. This dining room, for various reasons will be subdivided, so that it can conveniently accommodate boys and girls separately. Associated with the kitchen will be the hospital stores. Finally, a suitably designed school building (figs. 1A and 4), specially adapted for the type of children sent to this hospital, will be provided. The education given will be on the individual system and consist mainly of occupational instruction, handicraft, and Nature study. Much of the school work will, on sunny days, be carried out in the open air, and the school rooms will therefore be arranged so that they can open to the south and the desks be easily moved to the open air.

The London County Council provides for the convalescence of a number of children of preschool age (2–5 years). At present it has no adequate arrangements for dealing with them satisfactorily as a class by themselves. In spite of Sir Henry Gauvain's experience the Council proposes to try the experiment of providing a small unit for them at Littlehampton. They will be separately housed and cared for, and it is proposed to provide them with a separate school on kindergarten lines (figs. 1A and 4).

It is hoped that the experiment may result in material advantage to the health and the physical and mental growth of these children.

Teachers and nurses will be responsible for supervising physical exercises in the open air, walks in the neighbourhood, paddling, and sea bathing.

There will be a nurses' home (fig. 1B), with messing and recreation accommodation, &c., for it is obvious that such a hospital will require a large staff of nurses. Some of the sisters must be skilled in dealing with children's and orthopædic diseases, and be able to recognize the early signs of infection, while others must be experienced in massage and the administration of light therapy, and in remedial exercises.

The teaching staff will have to take part in supervising the children who are up, not only during school hours, but also during the evenings until they are ready to go to bed, so they will require sitting-rooms and messrooms (figs. 1A and 4).

A resident medical superintendent (fig. 1B), who must be an expert orthopædic surgeon, will be essential, and he will require the help of two assistants, preferably women, who will not only have to carry out the usual medical treatment but also interest themselves in research.

Such a hospital, situated in congenial surroundings protected from cold winds and rain, designed to deal with types of disease likely to profit by open-air treatment, and providing, under skilled supervision, the advantages of a health resort, will be a convalescent hospital in the full sense of the term.

In conclusion, I would like to record my grateful thanks to my various colleagues of the London County Council ; to Mr. W. L. Parry for advice and assistance during

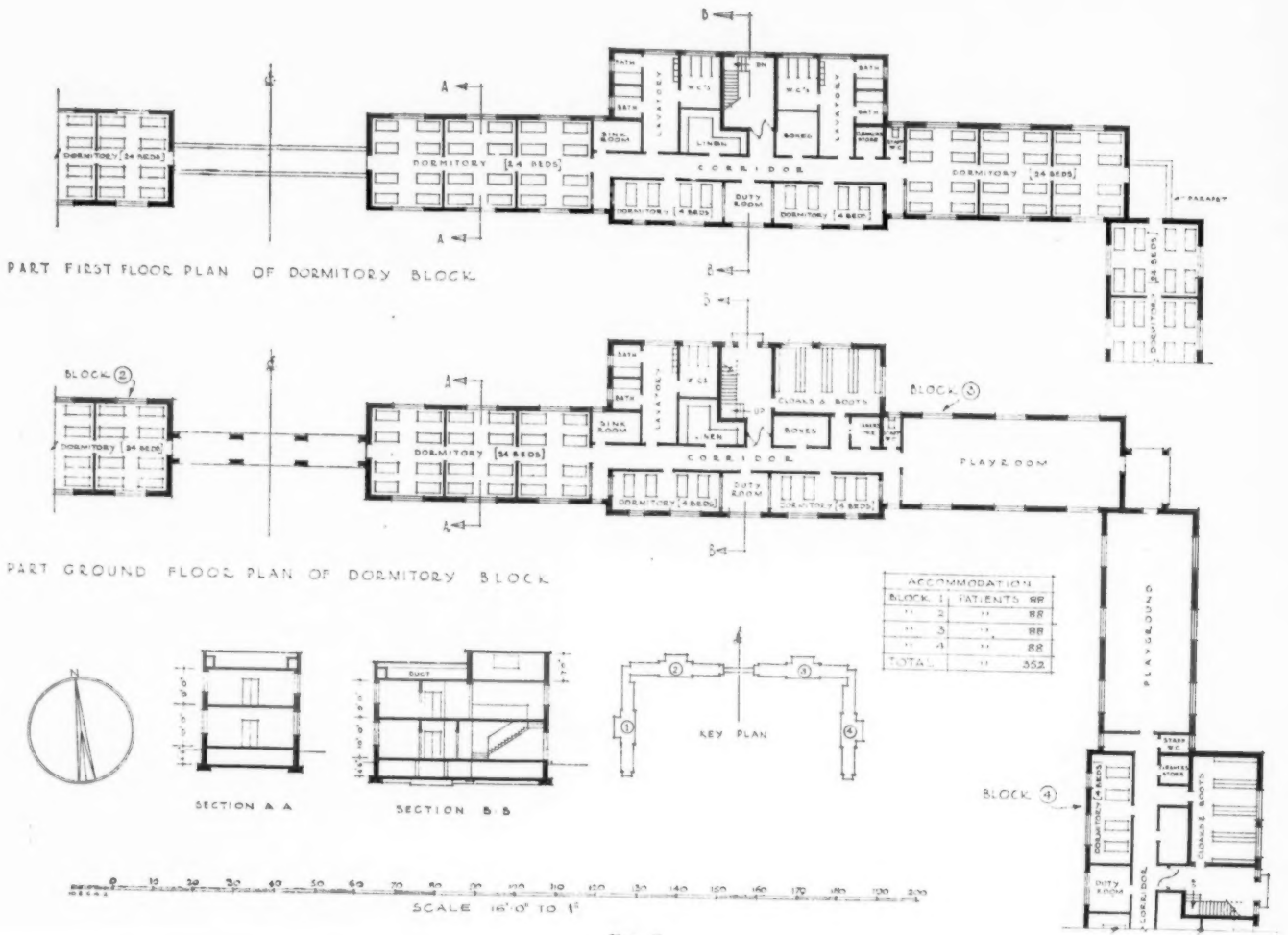

PART FIRST FLOOR PLAN OF DORMITORY BLOCK
PART GROUND FLOOR PLAN OF DORMITORY BLOCK
BLOCK (2)
BLOCK (3)
BLOCK (4)
DORMITORY (24 BEDS)
DORMITORY (34 BEDS)
DORMITORY (4 BEDS)
CORRIDOR
LAVATORY
BATH
W.C.'S
SINK ROOM
LINEN
BOXES
CLOAKS & BOOTS
DUTY ROOM
PLAY ROOM
PLAYGROUND
PARAPET
ACCOMMODATION
BLOCK 1 PATIENTS 88
" 2 " 88
" 3 " 88
" 4 " 88
TOTAL " 352
KEY PLAN
SECTION A A
SECTION B B
SCALE 16'-0" TO 1"

FIG. 2.

SCALE 16'-0" TO 1"

FIG. 2.

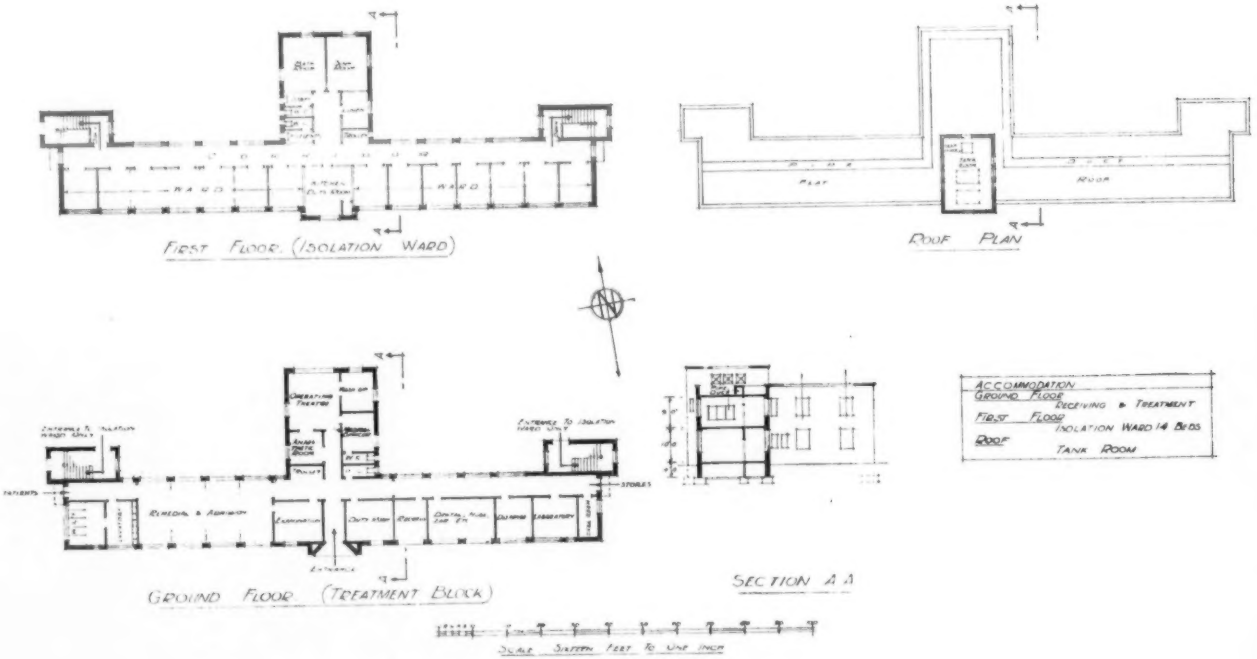


FIG. 3.

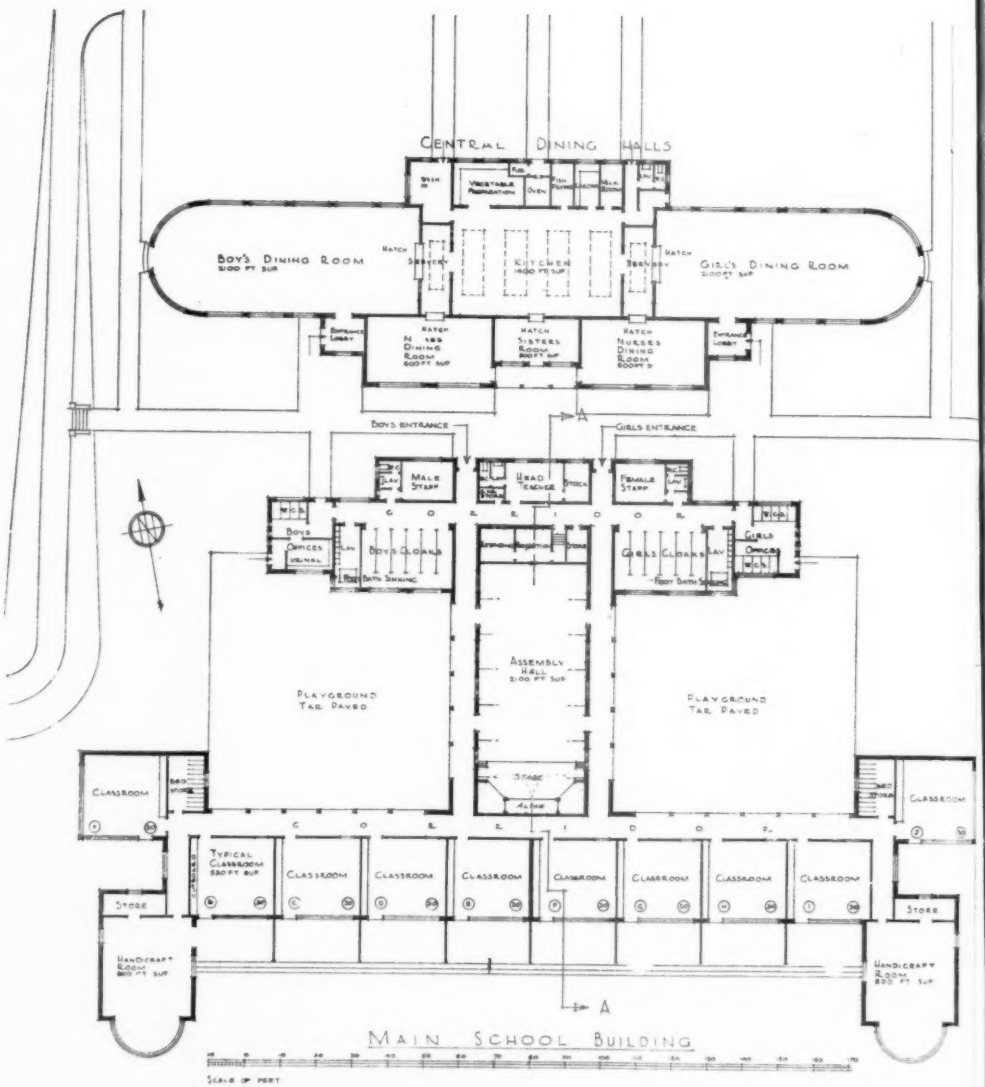
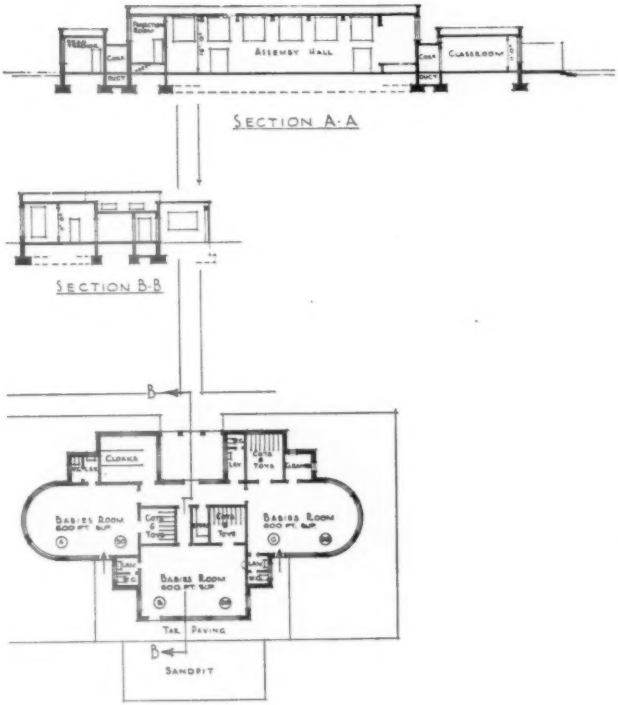

CENTRAL DINING HALLS
BOY'S DINING ROOM
KITCHEN
GIRL'S DINING ROOM
BOYS ENTRANCE
GIRLS ENTRANCE
MALE STAFF
HEAD TEACHER
FEMALE STAFF
BOYS CLOAKS
GIRLS CLOAKS
ASSEMBLY HALL
PLAYGROUND TAR PAVED
PLAYGROUND TAR PAVED
CLASSROOM
TYPICAL CLASSROOM
STORE
HANDICRAFT ROOM
MAIN SCHOOL BUILDING
SCALE OF FEET

FIG. 4.



ACCOMMODATION TABLE	NO. OF PUPILS
MAIN SCHOOL BUILDING	
NO 1 CLASSROOM AT 30 (820FT SUP EACH)	300
NO 2 HANDICRAFT ROOMS AT 30 (800FT SUP EACH)	60
ASSEMBLY HALL (2100 FT SUP PLUS STAGE	
TOTAL	360
BABIES SCHOOL	
NO 3 CLASSROOMS AT 30 (600FT SUP EACH)	90
GRAND TOTAL	450
CENTRAL DINING HALLS	
NO 2 PATIENTS DINING HALLS AT (2100 FT SUP EACH)	
NO 2 STAFF DINING ROOMS AT (600 FT SUP EACH)	
SISTERS DINING ROOM 300 FT SUP	
CENTRAL KITCHEN 1400 FT SUP WITH STORES ETC. IN ADDITION	

MILLFIELD, RUSTINGTON, SUSSEX
SCHOOL AND CENTRAL DINING HALLS

FIG. 4.

the preparation of this paper ; and to Mr. Hiorns and his colleagues of the Council's Architect's Department, for the plans and diagrams prepared by them to illustrate the planning of the ideal convalescent hospital.

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JOINT DISCUSSION No. 1

Section of Medicine with the Section of Therapeutics and Pharmacology

Chairman—H. L. TIDY, M.D. (President of the Section of Medicine)

[*October* 25, 1938]

DISCUSSION ON BENZEDRINE: USES AND ABUSES

Dr. Ivor J. Davies: In the *British Medical Journal* of September 25, 1937, I reported a case of acute aplastic anæmia following the self-administration of 190 mgm. of benzedrine in the course of nineteen days. Severe cardiovascular collapse occurred the day after the last dose had been taken. This was followed by gradual recovery and restoration to normal health. The patient said the drug was being used to some extent by persons studying for examinations. It was recommended that the sale of the drug should be more strictly controlled by its inclusion in the Poison Schedule. The subject of this report has remained in excellent health during the last twelve months.

Meerloo [1] reports similar cases of the use of benzedrine by students preparing for examinations and fully confirms my own opinion as to the inadvisability of allowing the drug to be obtained by the lay public without restriction. Apfelberg [2] reported a case of acute benzedrine sulphate poisoning in which severe cardiovascular collapse occurred with coma and convulsions. For thirty-six hours the patient was in an extremely grave state, but gradually recovered. This case was a psychoneurotic and had taken about 140 mgm. Although this patient recovered completely, it is obvious that benzedrine sulphate may be fatal in certain individuals in far smaller doses than would be expected from the ratios deduced from animal experiments. There appears to be some relationship between autonomic vasoconstriction caused by large doses of benzedrine and the convulsive attacks experienced by this patient.

Gwynn and Yater [3] gave half of a large group of students 10 mgm. benzedrine tablets after breakfast and lunch for three days; the other half were given tablets of lactose. After five days the preparations were reversed, but the students were not informed of this. Altogether 147 took benzedrine and 151 lactose. All of the former reported reactions of some kind from the use of the drug, while of the latter group only 16 reported reactions thought by them to be due to the (lactose) tablets. After a detailed description of the effects of benzedrine the authors conclude in general that the use of the drug might be permitted or even prescribed for normal persons suffering from lack of self-confidence or mild depression who deem it advisable to overcome these drawbacks temporarily, and in other conditions requiring mental alertness. They consider the use of the drug as only an emergency measure; there should be an adequate period of rest after the emergency has passed. They say the drug is apparently not habit-forming. While it does not appear to be dangerous, a

dose of 20 mgm. is probably excessive for the average normal person because of the insomnia and other unpleasant after-effects. The authors deal fully with the contra-indications to the use of the drug.

J. Hill [4] studied the changes in pulse-rate, blood-pressure, and subjective sensations in 20 normal subjects after benzedrine sulphate. From a study of 100 cases of sea-sickness treated with this drug alone or combined, he concluded it had great possibilities of usefulness in certain cases of sea-sickness where there were signs of excessive vagus activity.

Boyd and Ford Connell [5] consider that benzedrine relieves the symptoms resulting from nasal turgescence, but does not shorten the duration of the common cold. Benzedrine sulphate is slightly more toxic to the mucosa than either ephedrine or epinephrine. Pharmacologically benzedrine appears to act on the motor sympathetic, but also to some extent directly on the smooth muscle. Its vasoconstrictor powers are similar to those of ephedrine, but less than those of epinephrine. In a later communication Boyd [6] reports the effect of benzedrine on ciliary movement. In concentrations of 0·05 and 0·1% in distilled water he found the following sympathomimetic compounds had a depressant effect on the ciliary movements of the œsophageal mucosa of the frog, namely benzedrine, benzedrine sulphate, ephedrine hydrochloride, and meta-synephrine or neo-synephrin hydrochloride in order of decreasing activity. The author wonders whether the harmful effects of these substances on mucous surfaces, which are probably slight from single applications, should be ignored in view of the immense relief experienced by the patient. The fact that congestion of the nasal mucosa may be Nature's method of combating colds is a further subject for consideration. The situation may be similar to that of the antipyretics in the treatment of fever, antipyretic drugs being less considerably used now than formerly.

Davidoff and Reifenstein [7] report that they found the physiological action of benzedrine " variable, uncertain, unpredictable ". In their investigations 10–30 mgm. of benzedrine sulphate were given daily and the fluid intake reduced to 2,000 c.c. Hourly observations were made of blood-pressure, pulse, respiration, temperature, and vaso-motor reactions, and the daily variations in total urine, stools, weight, basal metabolic rate, knee-jerks, and cellular elements of the blood, were noted after several days. Ten cases were studied.

Detrick [8] and co-workers have confirmed the stimulant effect of benzedrine on the central nervous system, respiration, and blood-pressure.

Nathanson [17] noted that a decrease in weight was not uncommon during treatment with benzedrine. This is probably due to the increased activity induced by the drug together with decrease in appetite. Myerson and his colleagues [9] found that in the human alimentary tract, in contrast to the results in animal experiments, benzedrine produced prompt relaxation of spasm. They have used it since in treatment of spasm of the pylorus and colon. Rosenberg and collaborators [10] describe the limitations of benzedrine sulphate in the treatment of spastic colon. They treated 18 patients with spastic irritable colon with benzedrine sulphate ; of these 3 improved, 1 improved and then relapsed, 11 were unimproved, and 3 were worse. They consider the lack of uniformity of the effects of benzedrine on the spastic colon restricts its clinical usefulness to a considerable degree. They also found in two normal subjects and in the dog that benzedrine sulphate produced pylorospasm and enterospasm that prolonged the emptying time of the stomach and intestine. They do not recommend benzedrine sulphate in the treatment of spastic disorders of the gastro-intestinal tract.

Davis and Stewart [11] conclude that benzedrine sulphate, combined with the belladonna group of drugs or alone, is a very useful form of medication in post-encephalitic Parkinsonism. While it may not produce the striking relief of symptoms seen with the atropine group, it has the following advantage that the patient does not require increasing doses, nor does benzedrine show the distressing side-effects

frequently seen with the belladonna group. Dressler [12] had remarkable results with benzedrine in a case of Parkinsonism of seven years' duration and advocated its use in all types of Parkinsonism.

Matthews [13] found that in 20 patients with chronic encephalitis showing a Parkinsonian syndrome benzedrine sulphate given over a period from six to twelve months produced in 75% definite symptomatic improvement. The symptoms beneficially affected were not the same in every case, but on the whole there was lessening of rigidity, tremor, salivation, and oculogyric crises. In addition there was improvement in mood and an increase of strength and energy. He found that benzedrine enhances the effect of stramonium, atropine, and hyoscine, and was best used in conjunction with these drugs in the treatment of post-encephalitic Parkinsonism.

Solomon and Prinzmetal [14] have also described the results obtained in some 28 cases of post-encephalitic Parkinsonism with classical symptoms.

Bradley [15] reports the results obtained in 30 behaviour-problem children who received benzedrine sulphate for a week and were observed for that period. There was a spectacular improvement in school performance of half of the children ; this was a most remarkable effect. A large proportion of the chikdren became emotionally subdued and a variety of other behaviour changes were also noted. On an average a single morning dose of 20 mgm. was given. All the changes appeared promptly on the first day of the treatment and disappeared on stopping the drug.

Woolley [16] studied the effects of benzedrine sulphate in mental patients with retarded activity and found that of 70 patients falling in the groups of the various functional disorders 25% of all the patients in all groups were improved by administration of the drug. Patients who reacted favourably showed practically immediate improvement after 10 mgm. doses over a period of one to three days, which can probably be used as the best index of what is to be expected. Lack of response or unfavourable response to small doses should be taken as a contra-indication for the drug. Benzedrine sulphate properly administered in cases of extreme depression and retardation *may on occasion* determine the difference between prolonged serious illness and fairly prompt recovery. A large number of retarded patients can be materially benefited as regards their feelings of well-being and their initiative. On the other hand promiscuous and uncontrolled use of benzedrine is to be condemned ; the administration of the drug, as Bradley states, is not without its attendant dangers. These results are similar to, but not so optimistic as, those of other writers, and few have given sufficient warning as to the unfavourable effects which may be encountered in many patients even with small doses.

In conclusion, I consider that benzedrine must now be admitted as a useful drug in the treatment of certain mental disorders. There are undoubtedly risks of severe reactions from its effects on the circulatory system, but these may be lessened or removed by the use of smaller doses. The drug should always be given in the smallest dose necessary to produce the desired therapeutic effect. Benzedrine is undoubtedly a valuable addition to our therapeutic armamentarium. No remedy has hitherto had such satisfactory effects in certain types of depressive mental afflictions. The drug is to be placed in Schedule I of the Poisons Act, and personally I think restriction for the present should go even further, and it should be placed in Schedule IV of the Act.

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Dr. E. Guttmann: The experience upon which this contribution is based has been gained at the Maudsley Hospital, and I should like to thank Professor Mapother for allowing me to make use of the clinical material there available and to thank the Medical Staff for their kind co-operation.

After Prinzmetal and Bloomberg had discovered the value of benzedrine in narcolepsy, Myerson tried it in states of exhaustion and fatigue. At the same time Peoples and Guttmann, while studying the psychological accompaniments of variations in blood-pressure, experimented with benzedrine, and observed certain psychological changes. It has since been shown that the psychological changes were not correlated with the changes in blood-pressure, but must be regarded as a specific effect. Similarly, it also seems now to be proved that the psychological effects of benzedrine are separable and distinct from its anti-narcoleptic or sleep-disturbing properties.

Despite the difficulties associated with the finding of suitable normal individuals for such investigations, the following psychological effects may be described as the normal response to small or medium doses of benzedrine, 5 to 20 mgm. by mouth: a feeling of well-being, an agreeable sense of relaxation, and sometimes a more or less marked cheerfulness. Others, however, show an increased irritability of which they may or may not be aware. The pleasant effects are more marked, if such phenomena tend normally to be unusual for the individual. Thus the constitutionally depressed feel a little more happy; the naturally diffident more confident. A sense of energy and increased activity accompanies the increase of self-confidence and mild elation. Here, again, the fatigued and weary benefit more than others. To quote Myerson "the tired feeling around the face and the eyes which is perhaps the most disagreeable consequence of insufficient sleep and rest disappears", and all his subjects agreed that "to dissipate the hangover of a disordered night's sleep, or of insufficient rest the use of the drug is worth while". The feeling of increased activity is accompanied by objective evidence of increased motor activity and shortening of the reaction time. Some feel particularly that their capacity to take decisions is greater; this again is probably best seen in those who normally experience difficulty in this respect. Increased activity is most marked in the field of speech, and it was in fact the talkativeness of our subjects that originally drew our attention to the psychological symptoms. The flow of words indicates an increased production of associations and a speeding up of the thought processes, of which the subject may or may not be aware. This can be demonstrated by continued addition or concentration tests, by association experiments and tests for memory. The increased number of associations facilitates learning and reproduction. On the other hand, retention of material for a longer period often becomes worse (Reitmann).

The dividing line between improvement and impairment is nowhere more difficult to draw than in the field of attention and concentration. Thus some relish their increased wealth of associations, while others complain of lack of concentration and feel jumpy and distractible and in fact are so. Whereas the subjects may be able to do a larger number of simple additions mechanically in a given time, they may be

much slower in solving more complicated problems because of their difficulty in concentration. This effect can be very marked after a slight overdose. An alteration in the sense of time is another symptom of the changed activity feelings. The subjects say that time passes more quickly, and when they are asked to repeat a given time interval the intervals tapped become shorter; owing to the increased number of associations in a given time interval the interval appears subjectively longer than it really is.

It may be worth while to mention certain effects which are *not* produced by benzedrine. There is no measurable improvement in sensory perception, no evidence of sexual excitation nor impairment of moral inhibitions nor (in experimental doses) any evidence of clouding of consciousness. Anderson observed some dimness of vision, changes of sensation in the finger tips, fullness in the head and dizziness, in some of his subjects after doses of 20 mgm., and one of Davidoff's cases felt " groggy ". All these symptoms were probably evidence of a relative overdose. When the dose is large, the unpleasant bodily sensations generally predominate; motor restlessness and distractibility become trying; but, certainly with therapeutic doses, consciousness is not clouded.

The effect of a single dose usually wears off within a day, but some subjects experience a sense of well-being and a certain facilitation of associations and increased activity as late as the next morning, even after a sleepless night. These symptoms may be due to the prolonged action of the drug; Richter has found that excretion in certain subjects may not be complete at the end of twenty-four hours. On the other hand the feeling of lightness or fatigue or irritability the morning after a benzedrine experiment may be explained by the sleepless nights. The effects observed after the continued administration of small doses continue to be of the same type, but gradually become weaker in intensity. Five of the normal individuals given benzedrine for a period by Davidoff and Reifenstein showed increased irritability; two complained of lassitude after medication was stopped, and two others asked for more.

As regards the effects of benzedrine on patients, Sargant and Blackburn gave intelligence tests to a mixed group of patients and retested them after a dose of 20 mgm. of benzedrine. They found an average increase in score of approximately 8%. In individual cases it could be shown that the mental effects were independent of the bodily reaction or of the subjective experience of the bodily reaction. For example, a young man who suffered from a depressive state with anxiety features complained of very unpleasant subjective symptoms, increased palpitation and sweating, yet he actually showed a large increase in his score when retested. The patient himself explained this by saying that after he had taken the tablets he was able to overcome his feeling of hesitancy and make up his mind more quickly. The lack of correlation between the rise in blood-pressure and psychological effect has also been shown by Guttmann and Sargant.

Myerson and his co-workers gave benzedrine to 80 consecutive admissions (mainly major psychoses). No case showed any improvement, and 15 of the 80 cases showed a temporary accentuation of their psychosis. The method they employed, i.e. giving the drug indiscriminately to a number of admissions, is not a satisfactory way of obtaining any idea of the efficiency of the drug or the occasion for its administration. The statistical approach can certainly be most valuable, but it is only by studying individual patients or groups that a valid approach can be obtained.

There is now general agreement that benzedrine does not improve schizophrenic psychoses. It is true that a stuporose state has been helped in a few instances, but the same effect or a better one can be obtained by sodium amytal, which is much more reliable in its action. When depression disguises the essential symptoms, as can occur in paranoid and schizophrenic conditions, benzedrine is definitely contra-indicated. We have already warned against its use in such conditions. It is probable that the exacerbations seen by Myerson fall into this category. The man who jumped

from the seventeenth floor of a New York hotel was evidently schizophrenic and should not have been given benzedrine for this very reason. I have seen a favourable effect from small occasional doses of benzedrine only in two schizophrenics who were in a remission and showed some lack of initiative as the only residual symptom.

As we suggested in our first paper, the main field for the use of benzedrine is in the depressive states. Wilbur, MacLean and Allen, report that the immediate effect on depressions was striking in 70% of their cases, and 25% continued to receive benefit for a period of from one to eight months. The diagnosis " depression ", however, comprises such a variety of conditions, differing in ætiology and intensity and other features, that wholesale indications or contra-indications cannot be expected. All those authors who have analysed their cases beyond the mere diagnosis of " depression " seem to agree with, or at least do not contradict our previous statement that mild cases with marked retardation respond best. The psychomotor effect is more marked than the euphoric action of the drug (Davidoff and Reifenstein). This is in line with the previous experiences of trying to treat depression by means of drugs. None of the drugs producing euphoria that has been tried, such as cannabis and alcohol, improves the picture of melancholia. All observers agree that severe depression and depressive stupors do not benefit from benzedrine. Small doses have little or no effect and larger doses produce anxiety or untoward physical symptoms. Benzedrine seems to produce its best effect towards the end of a depressive attack (Sargant and Guttmann, Anderson). It may thus enable a patient to start work, or to take the initial steps towards social adjustment, earlier than he would otherwise be able to do. However, if retardation improves, whilst depression persists, the risk of suicide increases, whether this be in the natural course of the illness or as the result of therapy. We fully agree with Myerson that the psychological effects of benzedrine are best produced by small doses, and in many cases 2·5 mgm. given two or three times during the morning will produce far better results than one large dose.

The most difficult problems arise in regard to that type of patient whom I shall call psychasthenic. I have in mind the type of person who is easily fatigued and exhausted, and who is inclined to have abnormal reactions of either neurasthenic or hysterical type. Obsessional and hypochondriacal features are also common in these people, as are sexual anomalies. They are predisposed to all sorts of flight reactions, flight into intoxication, alcoholic or otherwise. Some of these people respond very well to benzedrine. Indeed, so well that they run the risk of addiction. Reifenstein and Davidoff observed such a tendency in those already addicted to alcohol, morphine, or other drugs. Anderson, however, was not successful in replacing alcohol by benzedrine in a depressive female psychopath who had been accustomed to large quantities of alcohol taken to overcome her inhibitions. Sargant and Guttmann pointed out the possible danger of the drug in forming addiction ; though the preponderance of disquieting somatic symptoms over the feeling of euphoria which occurs when large doses are taken, made us think that addiction would probably be rare. This optimistic prognosis has been justified, in spite of the Press publicity which regrettably followed our article. Only one case has been referred to me with the diagnosis of benzedrine addiction, and I would not even call her an addict in the strict sense of the word. This was the case of an asthenic woman, aged 40, a typist, who complained she had been in a state of exhaustion for many years. Somebody suggested that she should try benzedrine ; she did so and, having taken it, she felt " on the crest of the wave ", " ready for anything ". She became self-confident, forgot her worries, and felt that at last she knew what life could be ; she also felt more irritable than was her wont. She took 10 to 25 mgm. daily for seven months. During all this time she felt fine and did excellent work. In fact she did too well, for she incurred the jealousy of another worker in her office and had to leave. This happened, however, more than three months before she attended the Maudsley Hospital, and, in view of her personality, her tale must be taken with a grain of salt. This patient

gave up the drug without much trouble, did not describe any deprivation symptoms, and has never since made any attempt to get a further supply.

Chemical investigations kindly carried out for me by Dr. Richter showed that she excreted the average amount of benzedrine in the average time, i.e. at the time of the investigation her organism had no increased capacity for metabolising the drug.

The mere possibility of habit formation, however, suggests that the drug should be kept from the open market, as we have already advocated. On the other hand the danger of habit formation is obviously not so great as to discourage the use of benzedrine after careful consideration of the individual case.

Benzedrine is a stimulant, and although it does not appear to alter a depression fundamentally, it can lead to a symptomatic improvement which may tide the patient over a critical period, or it may provide that final impetus which is so often necessary in a depression that drags on.

It should be used even with greater reserve in cases of morbid exhaustion or chronic fatigue, where it is usually rest rather than stimulation that is required. One should, of course, warn normal individuals against the excessive use of this stimulant as against that of any other. But in states of morbid fatigue it may at times help a patient to take one of life's hurdles, and indirectly, by increasing his self-confidence, benefit him for a period beyond that of the actual administration. It is certain that not even in these two conditions is benzedrine the ideal remedy. There are, in fact, very few drugs available in the medicinal treatment of emotional reactions, especially in that of anxiety, though a really efficient and not dangerous substance for this purpose is badly needed in our therapeutic equipment.

The experiments with benzedrine suggest at least two lines of further research :—

(1) What are the psychological effects of other stimulant drugs ?

(2) What effect have changes in vegetative functions—induced by drugs or otherwise, on the emotional state ; or, in other words, how can one influence the emotions by attacking their physical accompaniments ?

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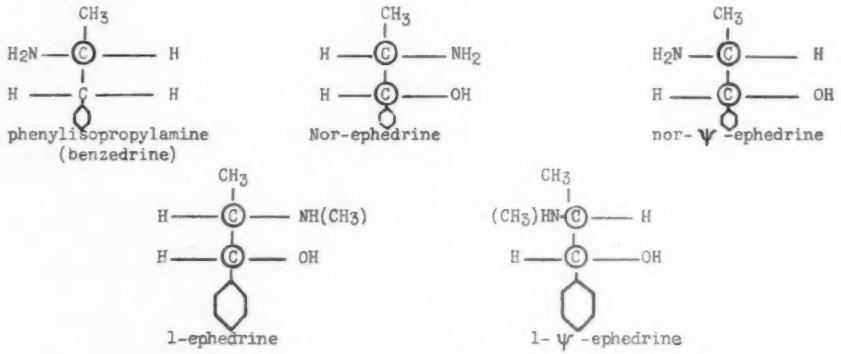
Dr. J. W. Trevan : I shall confine my remarks largely to the comparison of the analeptic activity of benzedrine and other compounds on animals (first noted by Prinzmetal and Bloomberg) on which we have done some work in my laboratory.

Benzedrine is the trade name[1] for a racemic mixture of d- and l-phenylisopropylamine $C_6H_5CH_2.CH\ (CH_3).NH_2$. The optically active carbon atom which is printed in heavy type, is the one attached to the NH_2 group. The relation of the compound

[1] The nomenclature of this compound is likely to lead to difficulties if it should ever be included in an official formulary. Isomyn has been suggested but has not met with much recognition. Phenylisopropylamine, as used later in this paper, is merely a convenient laboratory term not suitable for general use.

to the ephedrine group is shown by the formula for nor-ephedrine $C_6H_5.CH(OH).CH(CH_3)NH_2$ where two carbons are optically active and in consequence four spatial isomers are possible, d- and l-nor-ephedrine and d- and l-nor-pseudoephedrine. Ephedrine proper has one CH_3 group in the amino group $C_6H_5.CH(OH).CH(CH_3).NH(CH_3)$ and also has four isomers. The graphic formulæ of these compounds may perhaps make these various interrelationships clearer.



We have compared the optically active components of the benzedrine, the corresponding methylamino and dimethylamino compounds, and the four isomers of norephedrine, of ephedrine, and of methyl ephedrine, and compared them with picrotoxin and cardiazol.

The experiments were carried out on mice anæsthetized with paraldehyde. The anæsthetic was administered intravenously in a 4% solution in 0·9% saline. The various analeptics under examination were dissolved in the paraldehyde solution and a control group of animals was injected with paraldehyde alone in all except one experiment. Groups of 20 or 30 animals were used. As each animal was injected the time was noted by an assistant and the animal placed in a numbered square in the bottom of a box large enough to contain 30 animals and kept at a temperature of 25° to 30° C. The mice became anæsthetized within a few seconds and were watched continuously by a third observer until such time as the animals had wakened sufficiently to begin walking about. The time required for this I have called the walking time.

Fig. 1 gives the results of one such experiment in which a group of 30 mice injected with 0·064 mgm. of d-phenylisopropylamine dissolved in 0·4 c.c. of 1 : 25 paraldehyde were compared with a group injected with the same dose of the l-isomeride also dissolved in paraldehyde and with a group treated with paraldehyde alone. Each plotted point represents the duration of anæsthesia (walking time) as measured along the abscissa, for one or more animals out of the group of 30. The ordinates at any given duration represent the percentage of animals which were anæsthetized for that duration of time or less. There are some interesting statistical characteristics of these curves, the discussion of which must be left for another occasion. It will be seen that 50% of the animals recovered in twenty minutes after paraldehyde alone, in eleven minutes after paraldehyde and l-phenylisopropylamine, and in approximately six minutes after paraldehyde and d-phenylisopropylamine. It will be noted that these curves show a tail consisting of mice susceptible to paraldehyde and not so susceptible to analeptic activities.

When one methyl group is introduced into the amino group (phenylisopropyl-methylamine) a somewhat greater analeptic effect is shown. Fig. 2 shows the comparison of d-phenylisopropylamine and d-phenylisopropylmethylamine in equal

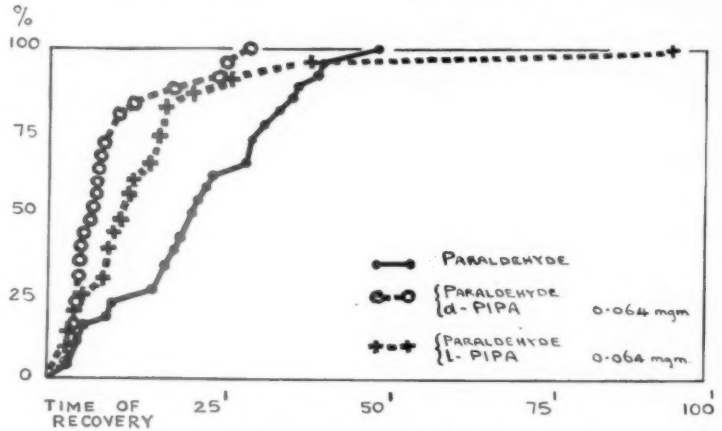


FIG. 1.—Analeptic action of d- and l- phenylisopropylamine.

Note.—Ordinate. Percentage of animals recovered. Abscissa. Recovery time in minutes. This applies to graphs 1–6.

doses. Again there is a " tail " of relatively insusceptible mice. A direct comparison of the d- and l-isomerides of phenylisopropylmethylamine shows the d-isomeride to be the more active.

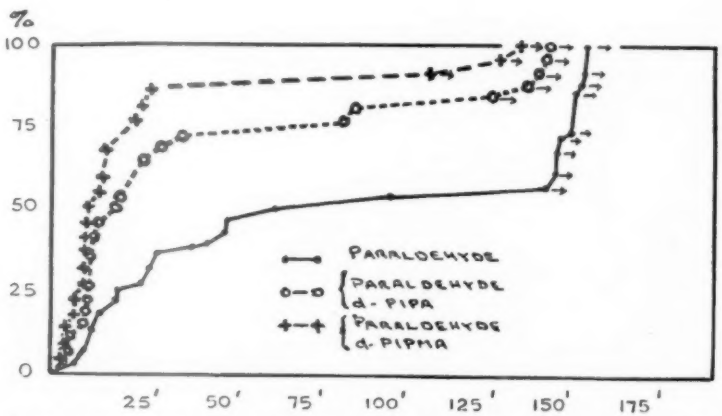


FIG. 2.—Analeptic action of d-phenylisopropylamine and d-phenylisopropyl-methylamine.

A second methyl group substituted for one of the amino groups destroys the analeptic activity of the dextro compound (fig. 3) and makes the lævo compound depressant. In the nor-ephedrine series the analeptic action was less, and with

ψ-ephedrine probably absent ; there was a less regular distinction between the optical isomerides. Where there was any, as with ephedrine, it was the lævo compound that was the more active.

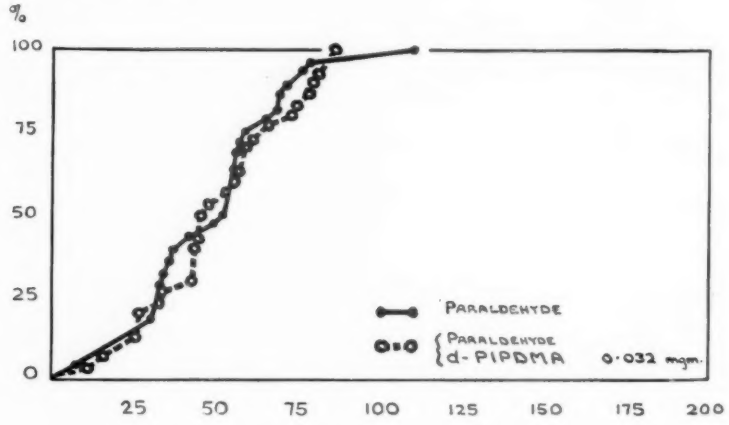


FIG. 3.—The action of d-phenylisopropyldimethylamine.

Fig. 4 shows an experiment with d- and l-ephedrine. The analeptic effect is striking, and suggests at first that it is not far inferior to that of phenylisopropylamine. This, however, is illusory. The relative effects of two analeptics can only be judged

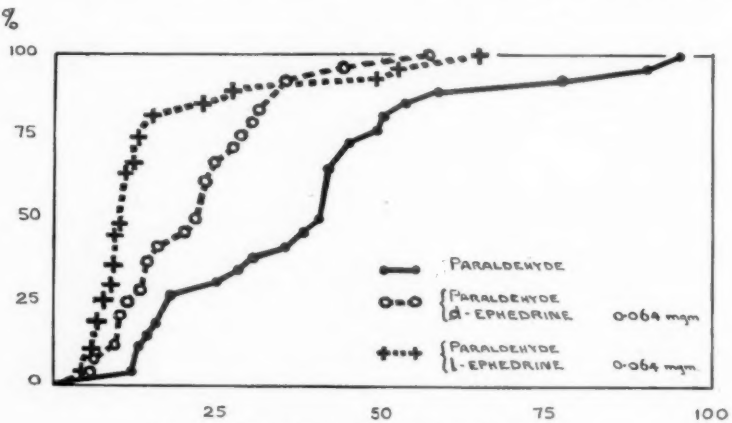


FIG. 4.—The analeptic action of d- and l-ephedrine.

by direct comparison carried out on the same day, as the sensitiveness of mice varies both to the anæsthetic and to the analeptic and the two variations are not correlated to any degree which we have been able to establish. The substitution of a further methyl group diminishes the analeptic activity as judged by recovery to the walking

stage. An estimate of the relative activities of the various compounds was made in the following manner. A series of dextro and lævo compounds of the phenylisopropylamine series were compared simultaneously by injecting with paraldehyde each day into groups of 20 mice.

TABLE I

Time at which half the mice recovered after the injection of 0·4 c.c. of a 4% solution of paraldehyde containing 0·032 mgm. of each of the drugs named. 20 mice in each group.

Drug	Walking time in minutes
d-phenylisopropylamine	20
d-phenylisopropylmethylamine	11·5
d-phenylisopropyldimethylamine	57
l-nor-ephedrine	38
l-ephedrine	31
l-nor-ψ-ephedrine	54
l-ψ-ephedrine	57
l-methyl-ψ-ephedrine	50

The results in the table give the times at which half the animals had recovered for each drug. It will be seen from this that, judging by complete recovery of the animals, phenylisopropylamine and phenylisopropylmethylamine are the most active, ephedrine and nor-ephedrine come next, and d-phenylisopropyldimethylamine, nor-ψ-ephedrine, ψ-ephedrine, and methyl-ψ-ephedrine, are least active. These last four have, in fact, shown little or no activity when compared directly with paraldehyde alone in other experiments.

There is another distinction between the phenylisopropylamine series and the ephedrine series. On recovery from anæsthesia the mice injected with phenylisopropylamine or phenylisopropylmethylamine show a characteristic motor activity. They run at great speed about the cages and dash themselves violently at the lids of the cages. Their movements are co-ordinated and accurate, but much more rapid than the normal exploratory trotting about indulged in by mice which are warm and comfortable. Mice recovering after the ephedrine series do not show this stimulation. The after-effect of phenylisopropylamine is probably due to the same kind of action as the various psychological changes reported for man and may be due to direct action on the cerebral cortex.

For comparison the experiments recorded in figs. 5 and 6 were made with three analeptics of a different type—cardiazol, picrotoxin, and picrotoxinin ; the last is the active half of the molecule of picrotoxin, which can be split up into inactive picrotin and picrotoxinin. When pushed to the limit above which convulsions are produced picrotoxin is at least as active an analeptic as cardiazol, and both awaken mice from paraldehyde sleep as readily as any of the benzedrine or ephedrine series. For the treatment of cases of anæsthetic poisoning one or other of these is probably to be preferred to any of the derivatives of phenylisopropylamine, and evidence is accumulating that picrotoxin has some advantage.

Both these compounds are convulsant poisons. In overdoses they produce epileptiform attacks quite different from the co-ordinated motor activity produced by phenylisopropylamine and phenylisopropylmethylamine. The site of origin of these convulsions is probably in the mid-brain. Picrotoxin, for instance, produces convulsions in cats decerebrated above the anterior corpora quadrigemina. We have therefore three groups of drugs, all of which awaken mice from anæsthetic sleep. Phenylisopropylamine, which produces marked signs of increased cortical activity but no convulsions, ephedrine which shows no other signs of central nervous stimulation than its analeptic activity, and picrotoxin and cardiazol, both of which produce epileptiform convulsions by acting on the mid-brain. To decide what is the common

factor in the three groups which antagonizes the action of the anæsthetic will need a great deal more research. The antagonism seems to be complete for cardiazol and picrotoxin respectively, for both these drugs show a reciprocal antagonism, in that not only do they antagonize the action of the anæsthetic, but can be administered

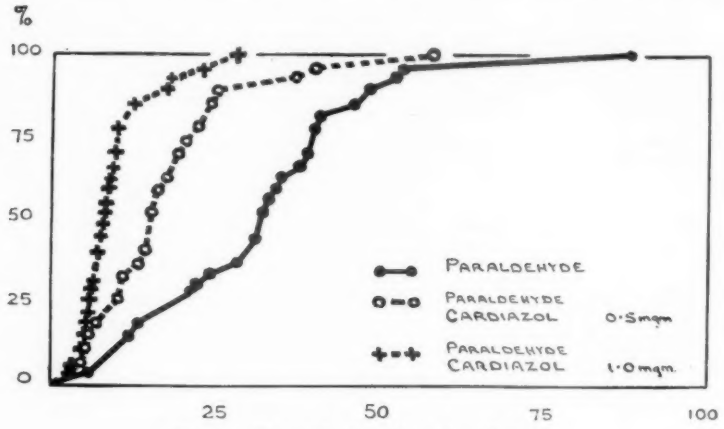


FIG. 5.—The analeptic action of cardiazol.

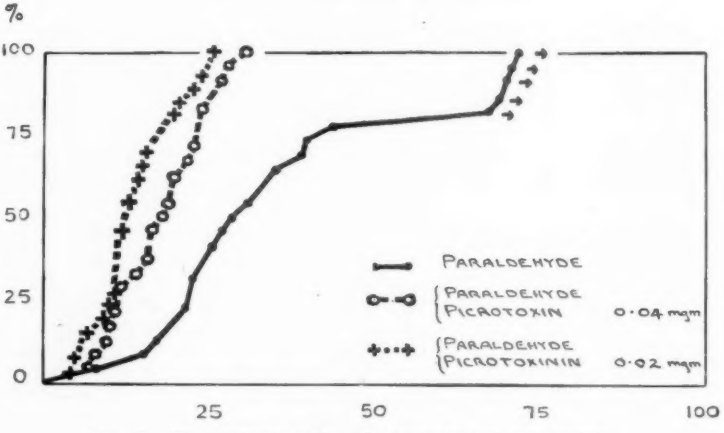


FIG. 6.—The analeptic action of picrotoxin and picrotoxinin.

to anæsthetized animals in doses which would be fatal to normal animals. This is not the case for phenylisopropylamine; it is, indeed, claimed by Hjort and co-workers that benzedrine is actually more toxic to the anæsthetized animal than to the normal animal.

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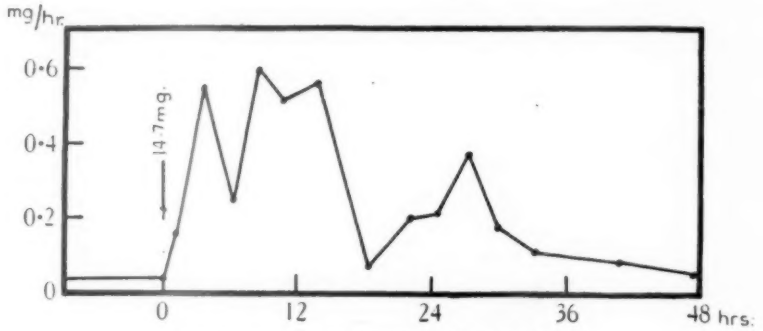
Dr. Derek Richter: Rate of elimination of benzedrine.—Amines such as adrenalin are known to be rapidly eliminated, but Dr. Guttmann has observed that the action of benzedrine sometimes appears to persist for more than a day. It has now been shown that the duration of action of amines in the body is determined mainly by the amine oxidase, an enzyme present in the liver, intestine, and other organs. Most amines are rapidly oxidized by this enzyme and therefore exert their action for only a relatively short time, but amines of the ephedrine series are not oxidized by this enzyme and are slowly excreted unchanged in the urine.

With ephedrine (26 mgm. base) approximately 100% is excreted in twenty-four hours, but with benzedrine (20 mgm. sulphate) and methylbenzedrine the rates of excretion are much slower, so that only about 40% is excreted in the urine in twenty-four hours and the excretion continues for some thirty-six hours after administration.



Rate of excretion of benzedrine (14·7 mg. base).

Dr. G. de M. Rudolf: During the administration of benzedrine to over 50 cases of mild depression without agitation in private practice, in the out-patient department of the Bristol Royal Infirmary and, under continuous observation, in Dorset House, the greatest benefit has occurred in those who are depressed in the morning and brighten later in the day. The patients should be asked a direct question such as: "Are you more miserable in the mornings or the evenings?", the last word being stressed to avoid the influence of suggestion as much as possible, as patients rarely refer to this matter spontaneously. A low systolic blood-pressure is a further indication for the use of the drug.

Individual tolerance is marked. Personally, I am very susceptible, a dose of 5 mgm. making me feel as if I swayed as I walked, although in reality I do not do so. A dose of 2·5 mgm. makes me more active and energetic, and I find I must restrain a tendency to talk and prolong lectures. Vertigo and unsteadiness of gait are certain symptoms of intolerance; restlessness and talkativeness those of a more advanced stage.

The commencing dose should be small, as 2·5 mgm. on rising. If only a slight effect, or no effect is seen, similar doses can be added at about 10.30 a.m. and 1.30 p.m., none being given later to avoid keeping the patient awake at night. Alternatively, the doses may be progressively increased by 2·5 mgm., but I have never exceeded three doses of 10 mgm. each. If this amount fails to produce improvement, I cease giving the drug.

In one case, although the patient reacted well to the dose, I was obliged to reduce it later. This apparently cumulative effect corresponds to the results obtained by Dr. Richter.

In another case the benzedrine ceased exerting any benefit after a few months' administration. Reports indicate that, in such cases, benzedrine will again diminish the depression after an interval free from the drug.

Dr. R. Ström-Olsen: For some time I have been treating certain types of neurotic patients with benzedrine in my out-patient clinics. Cases of neurasthenia and hypochondriasis, especially those associated with fatigue and lassitude, have shown good results. In anxiety neurosis, on the other hand, my results have not been good; I have found that where anxiety is present benzedrine is contra-indicated. I particularly remember two cases of anxiety neurosis with panic attacks who were rendered considerably worse and who showed marked exacerbation of their anxiety after a few days of the treatment.

JOINT DISCUSSION No. 2

Sections of Radiology and United Services

Chairman—H. K. Graham Hodgson, C.V.O., F.R.C.P.
(President of the Section of Radiology)

[*December* 8, 1938]

DISCUSSION ON RADIOLOGY IN WARTIME

Major D. B. McGrigor, O.B.E., M.B.: I will try to put before you the general practical application of radiology in wartime by discussing the adaptation of the Radiologist, his staff, apparatus, patients and environment to the radiological problems occasioned by traumatic surgery and medicine in war.

The nature of radiological work amongst the civil population in an emergency and its organization are still, as far as I know, unsettled. Projectile wounds may, however, be comparatively few.

With regard to medical war organization, naval or military, it is obviously impossible for one to speculate on the future of radiology unless one studies the two main aspects of radiology in wartime, viz. :—

(*a*) The specific contributions of past wars to radiology, and
(*b*) The specific contributions of modern radiology to future wars.

The two cannot be separated easily, so I will discuss them under six more detailed headings :—

(1) A short historical survey of radiology in wartime.
(2) Personnel : radiologist, radiographers ; duties, training, &c.
(3) Patients : class of, conditions of, traumatic disabilities.
(4) War wounds : necessitating radiological examination.
(5) Apparatus for service hospitals : specific and general.
(6) Localization of foreign bodies in wounds.

(1) *Short historical data.*—X-rays in wartime have been made use of since 1897, when it is recorded that a successful localization of a bullet in the lower end of a femur was made at Netley.

Case : Soldier from the N.W. Frontier of India 1895 had bullet wound in region of knee—this was localized *anatomically* to metal ball fixed on skin—a method in use to-day—surgeons operated and found bullet quite close to the site indicated, much to the surprise of the " X-ray officer " and surgeons.

Subsequent notes on the operation quote the use of trephine, gouge, chisel, and drill—hence the justifiable surprise of all. Again, on the Indian Frontier in 1898 coils were used in a temperature of 110° F. in the shade which sometimes melted both coils and plates ; but plates were made and Afridi missiles such as buttons and bits of telegraph wire localized. I note here for the first time the valuable observations of one entrance and two or more exit wounds. Passing on through the Soudan

War 1898, the Greek War 1898, the South African War 1900–02, the Indian Frontier again, the Great War, and several emergencies abroad since then, X-rays have been considered essential, but not always sufficient. Looking back on war experience and reflecting upon the merits and defects of the radiological services therein, we can now look forward to incorporating current radiological and radiographic progress both in initial preparedness and the manner in which development should proceed.

(2) *Personnel.*—In war the radiologist is the same as in peace, only the environment may be changed. The war front may be anywhere, and mobilizable radiologists no doubt wonder where they can best help, or under which category they can best register with the B.M.A. Central Emergency Committee or what other course to adopt such as joining one of the Supplementary Reserves.

The functions of the Central Emergency Committee are described in the *British Medical Journal*. Instead of several separate organizations with different conditions and varying responsibilities, we have one central body which will select and supply specialists and other officer medical personnel as required.

Radiologists likely to be employed in an emergency should have some idea of their possible duties before the emergency arises, and should have time to make their preparations, both private and professional. The services have their mobilization schemes always ready, and they will have available (*a*) serving radiologists; (*b*) radiologists on the Regular Service Reserves and on the Supplementary Reserves; (*c*) radiologists who register with the Central Emergency Committee for general service. Directors of medical services will thus have the necessary officer personnel for posting to commands at home and abroad and to special hospitals. As far as the Army is concerned, radiologists posted to mobilizing units will be given the opportunity to make themselves familiar with the standard apparatus and localization instruments as issued in the first place to service units, and with other apparatus, as they are mobilizing. Some of you may be attached to small mobile units, e.g. casualty clearing stations, and some to big general hospitals at home or abroad, but in the main the duties will be similar. An exception may be made with regard to special hospitals for particular classes of cases, e.g. eye, fracture, orthopædic, maxillo-facial, &c. Some may have to work in the tents (their only advantage is their mobility), and some may be housed in buildings ranging from "slums to luxury". Others may be in the wide-open spaces amidst dust, dirt, and heat, or may be detailed for hospital ships, either naval or military. One may even be sent to the tropics, where a good hot Indian summer teaches a radiologist quite a lot. In my own case I mobilized an Indian Field X-ray Section, as an independent divisional unit in India, in August 1914, and was working at full pressure in France in October 1914. Just compare this with your present day's work, a 12-in. coil, mercury break, make your own hydrogen, tubes various "green and greener", accumulators filled with sulphuric acid brought with you in glass casks, charged by a $\frac{3}{4}$ horse-power oil engine with blow-pipe ignition, working in a tent in the rain, using plates brought from England via an Indian store, yet we got good results sometimes, and with long exposures. Later I lived in luxury in a vacated school and took over from the French radiologist before me, the largest energizing Wimshurst I have seen. This illustrates the variety of location. Radiologists can be assured that wherever they may land, full use will be made of their special knowledge, but at the same time they will realize that they are primarily medical officers and occasions will arise when they must help with other duties. I well remember that my busiest time as a radiologist early in the War was when I had to close the X-ray Department and help with the general surgical and medical rush after a big battle. Radiologists in wartime must be prepared in many emergencies to do *all* the work *themselves*.

Radiographers and assistants.—As far as I know, immediate service needs can be supplied by serving radiographers and reservists. After that, I presume men and women joining for general service will be nationally classified and allotted to corps

according to their qualifications. I know of no special organization of the Registered Medical auxiliaries for war.

(3) *The patient in wartime.*—Your patients will mostly be previously healthy soldiers suffering from (*a*) compound fractures with big flesh wounds ; (*b*) comminuted fractures which have been immobilized ; (*c*) wounds infected by tetanus or gas gangrene ; (*d*) explosive wounds with injuries in vicinity of high-velocity shell bursts without penetration ; (*e*) retained foreign bodies : Bullets, shell, stones, equipment, &c. ; (*f*) effects of morphia and/or secondary wound shock. The care of patients under (*f*) is specially necessary and explains the "unusual patients".

X-ray departments will not be subject to overpowering rushes of work as this is regulated by the rate that surgical and medical units can make use of your help.

Many of your patients cannot be handled very much, and you may have to radiograph them on the stretcher on which they arrive, without altering their position.

(4) *War wounds.*—It has been said that the medico-surgical problems of future wars will be projectile wounds and emotional diseases.

The science of the motion of projectiles (ballistics) explains the causes and effects of war wounds.

The wounds, however, will not differ materially from those of previous wars. Shell wounds will predominate in defensive operations. Bullet wounds will predominate in offensive operations. The character of the wound or wounds (that is the dissipation of the energy) is determined principally by the velocity of the projectile, in lesser degree by its size, shape and instability ; and the density of the target hit.

(5) *Apparatus and accessories.*—Service classes include : (1) That stored in peace for particular units and purposes ; (2) that stored in peace in pool for developing units ; (3) that *not* stored in peace, i.e. mobilizable for mobilizing, stabilized, or special units or hospitals. Casualty clearing stations are the first complete operating and X-ray centres in the forward area, and we have the experience of them in the Great War to guide us. One is mobilized for each division, but they are not divisional units and are under the Director of Medical Services of the Army or corps ; hence their mobility and grouping (closed or open). The necessity of retaining certain operation cases for days in casualty clearing stations is established, providing the military situation allows of it, and therefore efficient X-ray service is needed in them. On the other hand in a future war I can picture conditions where the casualty clearing station may become an evacuation centre with very little X-ray work, because improved evacuation by rail, motor ambulance, and by air may reduce the stay of so-called immovable cases, e.g. sucking chests, penetrated abdomens, fractured femurs, &c. Thus the supply, packing for travel and storage in peace, of apparatus for this particularized unit with its specific changing surgical and medical demands, requires considerable care and foresight when all the facts such as military exigencies, mobility, portability, expansibility, location, economics, contracts, and completeness, are considered. The X-ray units for bigger and more stationary hospitals and hospital ships, apart from the mobile and portable sets allotted to start with, have already been carefully considered, and the situation is under constant review. As a result of experience, the tendency now is to classify and group wounded at the big hospitals ; a system which demands experts in special branches for each class and must include a radiologist. The advantages of this have been so apparent that it suggests the line of future work.

The Director-General of the Army Medical Services, in consultation with his Surgical and Radiological Staff, has approved of the following mobile and portable units for these specific and limited purposes :—

(*a*) Mobile units of 77 kv. and 15 ma. with tube and transformer, &c., oil immersed in a metal tank (there are special reasons for this particularly in the forward area) designed for rapid screening and filming with standard localization methods. These are packed in special transportable cases and carried in a standard mobile X-ray

lorry body which is also fitted for use as a dark room, and the table is specially designed to take a stretcher without moving the patient.

(*b*) Portable units of 90 kv. and 30 ma. are kept in a pool for issue or distribution as necessities develop, i.e. stabilization or grouping or special surgical or medical needs.

These two units are also available for the bigger hospitals, &c., in the first place.

(*c*) Large X-ray units or multiples for big or stable hospitals are not stored in peace time. The need for them is well known, and the most modern unit or units for particular types of hospitals and their location will be supplied. Multiple units have been adopted in case of damage and civil hospitals might note this. It is also hoped that types for particular classes of hospitals will fit in with the peculiarities of the various radiologists, who will have to adapt themselves to the selected apparatus supplied, as otherwise replacement services would break down.

Accessories.—These are listed, some stored, and others noted for supply. They are too numerous to mention, but include grids, screens, special gadgets for sinuses, face maxillary work, eye units, &c. The necessity for watching the progress in accessories is obvious, and to supply them where and when needed is economically essential. Standard localization methods are supplied as a basis for this work. Certain economical sizes of films are " turned over " regularly, and here I might say we have a great deal for which to thank the photographic research chemists.

(6) *Localization of foreign bodies.*—Dr. Ledoux Lebard divides localization methods into three parts : (*a*) Haphazard ; (*b*) precise ; (*c*) certain ; and, needless to say, he practises the third. I, however, will divide them into two : General and special.

General : The large number of wounds that have projectile fragments and other foreign bodies left in them forces us to concentrate upon simple and scientific methods for ascertaining their possible existence and location.

There are many slightly different technical procedures, pompously called new methods, which are almost invariably adaptations of localizations already described in the literature 1896–1900. Localization is only a matter of adapting simple established mathematical facts. Any experienced radiologist can do localization if he understands the mathematics of similar triangles, or of parallax, and can think in the three dimensions. Sometimes, however, it looks fascinatingly easy on paper and turns out just the reverse in practice. Anything like 100% accuracy is impossible, as the human body is not a motionless geometrical solid.

Without going into detail I will say that methods vary from simple to complex, for example from simple triangles and intersecting axes to the complicated Hirtz-compass, with stereography perhaps between the two in usefulness, and I must certainly add to these tomography. The double shift method for rapid screening, the Mackenzie-Davidson method for films and stereography, are the basic standard methods issued with service sets.

Localization reports.—They should be definite, and a complete report should be anatomical ; by which I mean you should adapt the mathematical data of the localization to surface markings or internal organs, bones, or tissues. This is best done by using a cross-section anatomy such as Symington's or Shoemakers', and plotting out the path of and the location of the foreign body, &c. I realize you cannot have a standard patient and adapt your patient to the cross sections, but you *can* adapt your sections to the patient's size. There are several ways of doing this, but the easiest is to have all your cross sections on a length of 35 mm. film ; you can then put them in an automatic focusing device and simply adjust the image to the patient's natural size. You now use your data by direct measurment and this gives the organ, or tissue, and path to where the foreign body ought to be. Always include coexistent bone or other pathology and the exact position in which the patient was radiographed.

Finally, be present at any difficult foreign-body operations.

General localizations need only be accurate to 1 cm. except in special cases.

Special localizations, e.g. eye: Here precision work up to ½ to 1 mm. may be necessary. Eye cases in forward areas, apart from bigger head injuries, may be confined to hæmostasis until they reach hospitals equipped for their needs, where the staff have ophthalmic surgeons and where the radiologist will have the necessary apparatus markers, scales, charts, &c., for the purpose. Many radiological eye cases are not primarily eye cases, their eye disability is often days old with loss or dimness of vision resulting from small foreign bodies embedded with little evidence of injury. This is similar to peace-time work and perhaps the development of the big magnets rather give radiology here the second place, but when used localization needs the above precision, as nothing but an exact localization is of any real value.

There are several well-known methods of finding the position of the foreign body by mathematical data in three dimensions from the central corneal axis and the plane tangential to the cornea. Here let me stress the fact that in mathematical localization the circles representing the greatest diameter of the eyeball in three planes become progressively smaller as they are removed from the equator to the circumference. This *all-important* fact is not usually given the publicity it demands. The simple solution is a geometrical section of the globe at the level of the foreign body in the elevation which when shown in plan view gives the intra or extra globularity with precision and certainty. These measurements are invaluable if the surgeon operates; and the complete report in an eye localization also frequently furnishes the necessary indications for the route of extraction.

Before finishing I would like to mention to you Dr. Pirie's work on X-ray sensitivity of the retina as something really new. Opaque foreign bodies can be located by the patient himself. Non-opaque foreign bodies such as radiolucent glass can be seen by the ophthalmologist on examining the fundus when a powerful beam of X-rays is passed through the eye. Glass fluoresces to some extent under X-rays. There are many other ophthalmic adaptations of this, but they are not radiological in character.

Colonel J. Weddell, F.R.C.S.: From the point of view of the surgeon the legacy of experience in a previous campaign is not always trustworthy. For instance, following on the experience in South Africa, at the beginning of the Great War gunshot wounds of the abdomen were treated expectantly, and the mortality was extremely high. Gas infections and tetanus were practically non-existent in South Africa, but in the Great War rapidly assumed the utmost importance. Radiology in war depends largely on the requirements of the surgeon. Therefore it is necessary for us to follow the evacuation of the wounded from the firing line and have a knowledge of the principles of treatment of war wounds in the various stages. We have the units in the forward area—those on the lines of communication and at the Base; hospital ships, and hospitals in the United Kingdom. In the forward area are the field ambulance dressing stations at which first-aid and emergency treatment is required and no X-ray work necessary. The principle in treatment is rapid evacuation of patients in as good a condition as possible to the casualty clearing station. The casualty clearing station is the first operating centre in the forward area. In France they were 10 to 15 miles behind the firing line, that is to say beyond the range of severe shell fire. One's ideas of casualty clearing stations at the end of the Great War were that they were stationary units, as indeed many of them had become, but it must be remembered that a casualty clearing station is a mobile "tented" unit and as such must be prepared to follow the fighting troops in advance or retirement. Also the area of fighting may be in a civilized country where an electrical supply is available; or it may be in countries such as Egypt, Palestine, or Africa, and out in the blue. Therefore the unit must be self-supporting with all essentials combined with mobility. Surgical work at a casualty clearing station will consist of operations on all types of cases, many of whom will have to be evacuated after a

few hours, especially in periods of heavy battle fighting. It is hoped to be able to retain the more severe cases, such as penetrating abdominal wounds, severe fractures, severe head and chest wounds, for eight to ten days after operation. Normally the wounded will leave the casualty clearing station by ambulance train to a general or special hospital on the lines of communication. The help that the surgeon will require at a casualty clearing station from the radiologist is the localization of foreign bodies and the condition of fractured bones. Therefore apparatus with these points in view has been designed. There is no place for barium meal work, pyelography, cholecystography, &c.

With regard to the localization of foreign bodies at the casualty clearing stations : (*a*) There are hundreds of men still going about with pieces of metal in their bodies which have caused very little harm. It is neither essential nor in many cases possible to remove every piece of metal from the body. The foreign bodies that we fear the most are the fragments of missiles of relatively low velocity, that is to say bombs, hand grenades, and trench mortars. The wounds are frequently multiple, and the fragments are liable to carry pieces of clothing and gross dirt into the depths of the wounds, which almost invariably become grossly infected. (*b*) With regard to retained foreign bodies in penetrating wounds of the abdomen, there are some things which radiology cannot tell us ; it cannot tell us whether arteries or veins have been wounded. Now what kills patients in the early stages of penetrating abdominal wounds is hæmorrhage, and in the late stages peritonitis. It is valuable to know whether the foreign body is below or above the diaphragm and whether it is in the peritoneal cavity or not, but time taken up in localization should be reduced to a minimum.

The casualty clearing station is a unit of 50 beds and 150 stretchers, but can expand to a great many more. For instance, on the Somme in July 1916, 13 casualty clearing stations of the 4th Army dealt with thirty-six thousand wounded in three days. It is obvious that in conditions of heavy battle fighting, extra surgical teams are necessary, and radiological personnel and equipment must be correspondingly augmented. As far as stress of work is concerned, at a casualty clearing station the radiological examinations will depend largely on the number of cases for operation. What may modify work at a casualty clearing station is evacuation by air when this is developed, and this should prove particularly useful in evacuating the serious fractures and head wounds to somewhere well beyond the fighting area where the patients can remain until they are convalescent.

General hospitals and special hospitals on the lines of communication are in a different category, and here more powerful X-ray apparatus, which is capable of the usual routine radiological work, will be provided. Hospitals in the United Kingdom, including special hospitals for orthopædic cases and maxillo-facial wounds, will have apparatus capable of carrying out general radiological work and any modifications necessary for their special requirements.